



One f the murals by Diego Rivera in the entrance hall f the N tional Institute Cardiology in Mexico City illustrating the earlier history of the development of o knowledge of the heart and its diseases. (Kindness f Professor Ignacio Chavez a Signor Diego Rivera, Mexico City)

HEART DISEASE

FOURTH EDITION

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THE PIONEERS PAST PRESENT
AND FUTURE, IN THE STUDY
OF THE CAUSES OF CARDIO-
VASCULAR DISEASES

PREFACE TO THE FOURTH EDITION

Six years have passed since I prepared the third edition of this book. Despite the retardation of medical progress by World War II and its aftermath there have been sufficient advances in our knowledge and treatment of heart disease to demand a considerable revision of this treatise and the publication of a fourth edition.

We are at the end of an era covered by the second quarter of the twentieth century during which various preliminary skirmishes have been carried out with the help of a few new technics, physical, chemical, and physiologic, and of an expansion of methods, such as electrocardiography and roentgenology introduced years ago. Minor advances have been registered in the understanding and treatment of cardiovascular disease, but the main problems still elude us.

Thus, on the threshold of a new half century we face the full challenge, which we have come a long way to recognize as such. We must, and I am confident that we can, master during the next quarter century much, if not all, of the three greatest threats to the public health of this country and of much of the rest of the world, each one more important than any other threat of our day—namely, rheumatic heart disease, high blood pressure, and presenile arteriosclerosis, especially as it involves the coronary circulation.

The important, though relatively minor advances that have been made since the first edition of this book was published two decades ago need not increase its size very much since certain cardiovascular diseases and their treatment are now so well known and routinely handled that the chapters dealing with them can be somewhat abridged to make up for the more complicated types that are in the process of vigorous investigation. As our knowledge of heart disease and particularly of its prevention develops during the next quarter century under the increasing program of research we may hope that treatises on the subject in the future will become smaller and smaller as should current textbook chapters on typhoid fever and tuberculosis.

The arrangement of the book into four parts has been from its inception a practical and orderly method of presentation and will be continued in the fourth edition. Part I on Methods of Cardiovascular Examination and on Symptoms and Signs can be somewhat abridged to cover simply the most important features of these subjects and newer knowledge, since lengthy treatises on certain technics are needed and available in current medical literature. Chapters 4 and 5 on Physical Examination of the Heart Itself, Including Inspection, Palpation and Percussion, and Auscultation respectively have

been conveniently merged into one chapter Chapter 5 the earlier Chapters 1 2 and 3 having been renumbered 2, 3 and 4 respectively to make room for a new historical chapter (incorporating Appendix 1 of the third edition) with which this new edition begins. The chapter on Electrocardiography has been rewritten to summarize its present fluid status and current clinical application for detailed discussion of underlying physical and mathematical bases for further intensive research in this field the reader is referred to the monographs of the special workers therein. A brief account of the interesting new technic of electrofluorokymography has also been added in the chapter on Roentgenology although it might equally well have been put into that of cardiography per se, to which a brief account of ballistocardiography has been appended.

Part II on the Prevalence, Causes, and Types of Heart Disease continues to be, as it has been from the start twenty years ago, much the most important part of the book, not only from the standpoint of diagnosis and treatment, specific and empiric, but especially because of its fundamental importance with respect to the mechanism of each of the various causes, leading, we may hope to its eventual conquest. It is in this direction that attention and support in research by both private and public enterprise should certainly have the utmost priority since the sooner we understand the causes of disease, the sooner we can control them and, by reduction of their prevalence, cut down the present heavy need of hospitalization for elaborate study and often prolonged treatment. The aged will, of course, be increasingly with us and eventually this treatise might evolve into a text on geriatrics.

Parts III and IV on Structural Cardiovascular Abnormalities (pathology) and Disorders of Cardiovascular Function (abnormal physiology) are still necessary evils to consider and to discuss, but are of far less importance than the subjects of etiology and pathogenesis of Part II. We have, however of late improved our methods of treatment of myocardial weakness and failure, the victims of which will long be with us. One chapter (Chapter 31) namely that on Coronary Insufficiency including the symptom Angina Pectoris, has been dispensed with as superfluous since it is adequately incorporated under appropriate chapters earlier in the book, in particular Chapter 3 on Symptoms, Chapter 21 on Coronary Heart Disease, and Chapter 26 on Valvular Disease.

In the process of an attempt to keep this volume at reasonable size and expense I have asked the advice of many friends and associates with respect to limitation of one part of the book or another In view of the many different opinions expressed, I have come to the conclusion that it is necessary to compromise in order not to omit altogether parts of the book that seem to one or another of the readers of considerable value. A result of these considerations has been the decision to delete paragraphs here and there and particularly to keep the bibliography within a relatively small compass. A large bibliography had been prepared containing many new references, but to have published this in full would have expanded the book 150 pages or more. Therefore only the more important older references and some of the

newer publications have been retained to appear as previously at the end of each chapter Where a fairly large number of references are retained there continues to be a separation between publications prior to 1944 and those since 1944 and into the year 1951 for the convenience of readers of previous editions.

Again as in the case of previous editions the author wishes gratefully to acknowledge the invaluable help of his medical colleagues from near and afar and particularly of his wife and of his secretary Helen Donovan, in the preparation of this new edition. It is with great appreciation also that I acknowledge the advice of Dr Arlie V Bock of Harvard University Cambridge, Mass., who reviewed the proof The Macmillan Company has, as before, been most kind and thoughtful in their vital aid in its publication.

PAUL DUDLEY WHITE

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CHAPTER I

THE EVOLUTION OF OUR KNOWLEDGE OF THE HEART AND ITS DISEASES

INTRODUCTION

Human progress of the past is the foundation on which our present-day life is based. Some knowledge of it is essential for a proper balance in our understanding of any field of science or of art and for the development of plans for the future in research and growth. Medicine is no exception, and the study of cardiovascular disease and practice therein make up one of the largest and increasingly important fields in medicine. This fact is responsible for the introduction into this book of a new first chapter concerning the evolution of our knowledge of heart disease which had appeared in the last edition simply as an Appendix in the form of a table.

Not only is the history of medicine of importance culturally in the education of a physician and a source of pleasure and interest through the lifetime of anyone who has once fallen under its spell, but it has a practical value in revealing clearly the gaps in our knowledge and in presenting occasional clues or discoveries long forgotten and needing revival. "Men were not all cowards before Agamemnon or all fools before the days of Virchow and Billroth," said Oliver Wendell Holmes, and Lowell wrote,

> "'Tis man's worst deed
> To let the things that have been run to waste
> And in the unmeaning Present sink the Past.

In 1749 Senac mentioned the value of quinine in patients with rebellious palpitation. This was forgotten by succeeding medical writers, at least by those who influenced medical practice, and more than a century and a half elapsed before a Dutch patient of Professor Wenckebach rediscovered the value of quinine in the treatment of cardiac arrhythmia, soon to be succeeded by its more effective isomer quinidine, which we have used helpfully ever since.

In 1785 William Withering gave explicit directions for the correct dosage of digitalis, but with rare exceptions it wasn't until our own time that this advice of his was properly followed. Many more instances of this sort could

be presented to illustrate this neglect of what has gone before and thus to give an immediately practical reason for reading old books.

Priority is often an idle boast and not too much should be made of it. Unfortunately names of medical writers have often been attached to symptoms, signs or diseases and although it is sometimes of interest to refer to such individuals by name and date and to quote from their works, one must realize that often descriptions of these same symptoms, signs and diseases had already appeared in medical literature in the writings of authors not adequately recognized by their contemporaries or quickly forgotten by their successors, only to be rediscovered. One example of this is the congenital syndrome called the tetralogy of Fallot, although Fallot in 1888 described it as a clinical entity for the first time clearly it had already been recognized by Peacock in 1858 by Gintrac in 1824 by Farre in 1814 by Hunter in 1784 by Sandifort in 1777 and by Stensen (Steno) in 1672. I dare say that if we would take the trouble to peruse in detail every medical writing before Bonetus we would find still earlier priority Morgagni himself in 1761 described a case of the morbus caeruleus, a girl who died at the age of 16 and post mortem showed pulmonary stenosis, an atrial septal defect, and very large right ventricle and atrium So it goes in many instances of medical progress sometimes indeed *there have actually been momentary or even longer steps backward as well as forward.*

There is one other important consideration about priority in olden days particularly and that concerns the difficulty and delay of publication. Often new truths were presented by word of mouth, by lecture, or by demonstration long before they were printed thus Harvey taught *De Motu Cordis* for a good many years before his famous book appeared, Withering tested the effect of digitalis for ten years before he wrote a book about it, and Lancisi was dead eight years before his most noted work saw the light of day The long discussion as to whether Servetus or Columbus discovered the circulation of blood through the lungs has been inconsequential because neither one claimed it or gave evidence in quoted writings that he initiated the idea. They both wrote as if it were at that time (in the 1550's) a well-known fact, as it doubtless was. Although it has, in recent years, been ascribed to Arabian observers of a much earlier date, it actually is, in all probability lost in antiquity and the originator of the idea may never be discovered. Incidentally many of these discoveries come to pass very slowly one worker after another adding a stone to the edifice, as indeed happened in the case of the concept of the circulation of the blood, William Harvey supplying the final keystone to complete the arch.

This chapter perforce can do no more than to give a bird's-eye view and a broad outline of the development of our knowledge with notation of a few specific instances of landmarks and milestones along the way but it is my hope that it will prove helpful in setting the stage for what is to follow For details of medical history one should consult the bibliographies at the end of this chapter and of other chapters which deal with specific subjects, the chrono-

logic outline following this chapter the historic quotations that appear in later chapters of the book, and a historic chart prepared by the author first in 1933 and revised in new editions in 1937 and 1944

The recognition of heart disease as of clinical interest and importance was exceedingly slow In 1618 one hundred and eleven years after the pioneer publication by Benivenio of the pathologic findings in 111 postmortem ex aminations, including several of cardiovascular interest, and ten years before Harvey's *De Motu Cordis* there appeared a volume of 405 pages entitled *De Affectionibus Cordis (Libri Tres)* and written by Albertini. Ever since Galen, manuscripts on the pulse *(De Pulsibus)* had been written and rewritten by physicians and scribes, along with similar treatises on the urine, culminat ing after many centuries in the poems of Gilles de Corbeil *(Ægidius Cor bollensis)* written in the thirteenth century and published as two of the earliest printed medical works before 1500 *(incunabula)* appearing in 1484 and 1486 respectively General works on medicine, written or printed, such as that of Fernel of 1554 had similarly contained chapters on the pulse and urine as the only references to the circulation, normal or abnormal, over many many years and well into the seventeenth century Here at last with its imposing title, Albertini's book seemed to give promise in 1618 of something more, but careful perusal shows it to be but a very wordy successor of so many writings of centuries before, quoting in particular Aristotle, Galen, and Avicenna. Like Galen, Albertini did, to be sure, recognize the very fast pulse, the very slow pulse, pulses of all shapes and sizes, and arrhythmias such as atrial fibrillation although that designation was not, of course, used. Like others, he ascribed palpitation, faintness, and syncope to the heart and recognized reflex effects on the heart's action and on the pulse of trouble elsewhere in the body as in the stomach, uterus, lungs, or brain, but, beyond this, there was nothing of importance or new based on clinical observation or even on the autopsies which had been accumulating during the previous century and which had shown that it had been possible for some persons to survive for an uncertain length of time with chronic defects of heart or pericardium. Until autopsies at the start of the sixteenth century had shown this to be so, the belief had been universally held that death must result if anything at all serious happened to the heart. Thus heart disease, as we know it today was not recognized, and Albertini, doubtless representative of his time, stated as late as 1618 that the heart could not support any grave lesion.

So far as I have been able to determine credit for the first publication of the introduction of clinical observations of the effects of cardiovascular dis- ease belongs to Lower who while demonstrating for the first time the possi- bility of transfusion of blood from one animal to another including man (1665) was collecting data concerning the heart, normal and abnormal, which he got printed by the Elzevir Press in 1669 under the title of *Tractatus de Corde* This small, but very important, little treatise contains, among other items of interest, the first description of cardiac tamponade and constriction

by pericardial effusion and scarring respectively Soon after this, Lower's fellow countryman Mayow in 1674 published his *Tractatus Quinque* in which the oxygenation of the blood in the lungs is clearly presented Mayow's fifth treatise was one of the very earliest on rachitis.*

Mention should be made next of two other important medical writers of the last half of the seventeenth century who, although not dealing specifically with heart disease, contributed significantly to the subject. Kerckring in Amsterdam in 1670 wrote a treatise on pathology called *Spicilegium Anatomicum* in which, with apologies to his teachers and colleagues, he pointed out their grave error in considering as evidence of heart disease the postmortem clots found in the heart, by this one brief statement he altered radically the current misconception about the heart, wiping out doubtless fully one half of all so-called heart disease. The other writer who did so much at that time to elucidate somewhat the still very dark subject of heart disease, was Bonetus who in two editions of his *Sepulchretum* (1679 and 1700) presented, among more than two thousand other case reports with clinical notes and autopsy findings, several hundred whose symptoms and signs were to be ascribed to lesions of the heart and great vessels. These cases he collected from all possible sources they make an invaluable compilation which served as a basis for his successors, including Morgagni one hundred years later (*De Sedibus et Causis Morborum* 1761) In this rich clinicopathologic collection there were many firsts, involving all parts of the body There were the earliest associations of dyspnea with cardiac enlargement, sudden death with calcareous aortic stenosis, and collapse and early exitus with a high degree of coronary artery narrowing.

Early in the eighteenth century two important books on the heart and some of its diseases were published in France and Italy respectively by leading authorities of their day The first entitled *Traité Nouveau du Coeur* appeared in 1715 prepared by Vieussens who, in his youth thirty years before, had published a pioneer work on the nervous system called *Neurographia*. An excellent description of the mechanical effect of severe mitral stenosis on the lungs with resultant congestion and dyspnea appears in this work by Vieussens. The other writer was Lancisi, physician to Pope Clement XI, to whom he dedicated the volume entitled *De Motu Cordis et Aneurysmatibus* which was published posthumously in 1728 Lancisi described engorgement of the neck veins associated with dilatation of the right ventricle and discussed cardiac enlargement at some length. An illustration of the very rich nerve supply of the heart is included in this volume and was bettered only years later when in 1772 Neubauer published a drawing of a beautiful dissection of the sympathetic innervation of the heart. Lancisi was an able and prolific writer and had earlier published several books on medicine and other subjects, such as fungi. One of these medical books is unique in that it was entitled *De Subl*

* Since writing this I have within the last few months acquired still earlier work by Mayow fascinating booklet published in 1671 and entitled *Tractatus Duo Quorum prior agit de Respiratione: Alter de Rachitide* The first printing of this little book appeared in 1668.

tanels Mortibus (On Sudden Death) (1707) It contained autopsy reports of individuals who had died suddenly and whose postmortem examinations had been carried out at the express request of the Pope, an instance long forgotten of the liberal, enlightened, and scientific attitude of the Church.

Now we come at last to what is often called the first textbook on heart disease itself namely the *Traité du Coeur* by Senac published in Paris in 1749 It has much more of clinical and practical importance than had been presented by any earlier publications. This is particularly true of treatment, of which there was scarcely any before two hundred years ago Senac mentions the value of bleeding and sedation in heart failure and of quinine in rebellious palpitation, a very early forerunner of the relatively recent application of quinidine to the treatment of cardiac arrhythmia. Following Senac, various textbooks on heart disease have appeared in different languages, most of them, however after a delay of a half century or more. Included among them are in French those of Corvisart, Napoleon's physician (1806) Huchard (1889) Vaquez (1921) and Laubry the present leader of the French school (1930) in German those of Kreysig (1815) Traube (1856) Fraentzel (1889) Romberg (1906) Edens (1931) and Hochrein (1941) in English those of Hope (1832) Stokes (1854) Flint (1859) Steell (1906) Mackenzie (1908 4th edition, 1925) Hirschfelder (1910) White (1931 the present edition the 4th, 1951) and Levine (1936 4th edition, 1951) in Italian those of Testa (1810) and Luisada (1938) and in Spanish that of Cossio (1935 4th edition, 1949)

More important as a rule than these textbooks, however have been monographs on important new technics or on etiologic, diagnostic, or therapeutic discoveries, beginning with Auenbrugger's introduction of percussion in 1761 in a little book in Latin entitled *Inventum Novum ex Percussione Thoracis Humani* but not well known until Corvisart's translation in 1808 Percussion was further developed by Piorry (1828) and Skoda (1839) This was the first of the technics which have been slowly but steadily introduced into the practice of medicine to improve the diagnosis of heart disease. One of Corvisart's pupils was Laennec whose introduction in 1819 of the stethoscope for mediate auscultation of the heart and lungs was a very significant advance *(De l'Auscultation Médiate)* A century later Cabot and others began to try by electrical methods to broadcast by separate earphones or loud-speaker to groups and classes the heart sounds and murmurs of an individual patient and to record them on phonographic records, while simultaneously Lewis and others began to photograph on moving film by way of microphone and galvanometer the auscultatory findings with simultaneous electrocardiogram (phonocardiography) These technics slowly evolved to their present higher degree of usefulness with the help of Einthoven and Geluk, of Geckeler of Mannheimer and of Sprague and Rappaport.

One hundred years ago (1846) Hutchinson introduced the determination of the vital capacity of the lungs. Another interval elapsed before the fourth helpful technic in the study of the circulation came to pass this was the

sphygmograph which, first developed by Marey in 1860 gradually evolved into a practical instrument, the ink polygraph in the hands of Mackenzie who printed many of his graphic records in his classic on *The Pulse* in 1902 and who with the help of Wenckebach, called attention to the serious significance of pulsus alternans. The next important technic, namely the sphygmomanometer was slowly introduced by a group of workers (von Basch, 1881 Potain, 1889 and Riva Rocci, 1891) another decade or two passed before blood pressure measurement became a routine clinical procedure nearly two hundred years after the English parson Stephen Hales, had accurately measured the arterial pressure of a mare in 1733

Roentgen, late in 1895 announced the discovery of his x rays, and the following spring Williams of Boston published an x-ray picture of the heart. In this field there has been a steady advance ever since with the introduction of orthodiagraphy of the heart by Moritz in 1902 of teleroentgenography by Köhler in 1905 of roentgenkymography by Stumpff in 1931 (suggested by Sabat in 1913) with further development recently (1945) by Chamberlain, Henny and Boone, by application of photoelectric cell and galvanometric graphic recording of angiocardiography by contrast injections by Forssmann in 1931 Castellanos in 1937 and by Robb and Steinberg in 1938 and of roentgencinematography by Reynolds in 1934

Another technic of the greatest value has been electrocardiography The study of the electrical activity of the heart introduced nearly a hundred years ago by Kölliker and Müller (1855) was carried on laboriously in the physiologic laboratories for nearly fifty years before a practical instrument (the string galvanometer) was developed by Einthoven in 1903 to replace the clumsy capillary electrometer which had been employed by Waller in 1887 to take the first human electrocardiogram. Nearly another ten years passed before clinical electrocardiography began under the stimulus of Kraus and Nicolai in Berlin and of Lewis in London In the last twenty-five years there has been a considerable amplification of the use of the electrocardiograph in the diagnosis of heart muscle injury and especially by the application of unipolar leads to the chest wall itself.

Finally with regard to special diagnostic technics, one should mention cardiac catheterization, which, first introduced by Forssmann who experimented on himself in 1929 has now evolved, through the help of Cournand, Dexter McMichael Lenegre, and their colleagues, into a routine practical method of intracardiac and pulmonary artery blood gas and blood pressure measurements to aid in the more accurate diagnosis of congenital and other obscure cardiac defects.

Leaving the history of the introduction of the diagnostic technics which began with Auenbrugger's discovery of the value of percussion in 1761 let us proceed with other historic advances in our knowledge about heart disease, and first about symptoms In 1768 Heberden described angina pectoris and gave it its name although he did not connect it with the heart he knew that it was a dangerous symptom and that it was particularly likely to attack

middle-aged males its connection with coronary artery disease was discovered by Jenner about 1772 but not published by him until 1799 in a letter to Parry which appeared in the latter's book entitled *Syncope Anginosa*. Over one hundred years went by for some obscure reason, before the common coronary complication of acute thrombosis with myocardial infarction received adequate recognition as a clinical entity by Herrick in 1912, and still another decade passed before Herrick's notable contribution became widely known. Finally we owe much to Anitschkow for his demonstration of atherosclerosis in 1912, to Leary for his painstaking delineation of the lesions of coronary atherosclerosis (1935) and to Schlesinger and Blumgart for their valuable exposition of the evolution of the lifesaving coronary collateral circulation (1937–1941)

Although dyspnea had been associated for the first time with heart disease by Bonetus in 1679 having been considered a symptom solely of pulmonary or pleural disease before that time, it was not until Vieussens described the mechanism of dyspnea in mitral stenosis in 1715 and Hope that of breathlessness in myocardial failure a century later (1832) that the pathogenesis began to be understood. Senac and Hope in their noted textbooks in 1749 and 1832 called attention to the fact that asthma may be a complication of a failing heart with pulmonary vascular congestion. Only in recent years, as a matter of fact, has there been a renewed interest in this relationship. Still another type of disturbed breathing consisting of periodic apnea and dyspnea and associated with cardiovascular disease was described by Cheyne in 1818 and Stokes in 1854 *

Other symptoms than angina pectoris, dyspnea, and palpitation that can be credited to the heart are few but there is one that has been well described, namely syncope due to heart block and attended by a very slow pulse this goes by the three names of its chief observers Morgagni (1761) Adams (1827)-Stokes (1854) syndrome.

Many signs have been named after physicians but frequently not by any means after those who discovered them first or even described them best. Thus there is frequently an erroneous significance to such a designation where priority has been wrongly assigned. Where possible, not only for this reason but for others too, especially that of preference for a descriptive term over a proper name, it is more reasonable to drop the eponym and in the future not to add such to medical literature. Examples of both the reasons noted above are water-hammer instead of Corrigan pulse, and chronic constrictive pericarditis instead of Pick's disease the water-hammer pulse had been well known and described long before Corrigan, and Chevers had well described chronic constrictive pericarditis fifty years before Pick. There are exceptions, however in which the descriptive term is so long and complicated

* My attention has been called by Dr Arlie V Bock to the fact that Hippocrates probably referred to Cheyne-Stokes respiration in describing the case of man who died of fever in an extremely delirious state. This patient had unusual breathing It was referred to as follows: "The breathing throughout, as though he were recollecting to do it, was rare and large. (Hippocrates, Loeb Classical Library G P Putnam, New York, 1923 Vol. 1 p 187)

or the eponym so firmly established that the observer's name may wisely be retained.

As to abnormalities of pulse form and rhythm, descriptions were quite completely presented by Galen in the second century A.D. and by his followers for the next 1,500 years but it took many centuries before the explanation for the abnormalities was given. The water hammer pulse was attributed to free aortic regurgitation not only by Corrigan in 1832 but also by his predecessors and contemporaries. The first to ascribe the plateau or more importantly the anacrotic pulse to aortic stenosis is not clearly known as yet. The paradoxical pulse was described by Kussmaul in 1873 and attributed, when marked, quite rightly to pericardial disease. Extrasystoles were known to the ancients, but the first reassurance about them was given by Williams in 1835 and confirmed by Mackenzie in 1902. In 1887 Bristowe described paroxysmal tachycardia as a particular entity corroborated the next year by Bouveret after whom it has sometimes been called. "Auricular fibrillation" was identified as a clinical condition independently by Rothberger and Winterberg and by Lewis in 1909 while "auricular flutter" was accurately described and named by Ritchie in 1911

After the introduction of auscultation by Laennec, abnormalities of the heart sounds and heart and blood vessel murmurs began to be described and explained. C J B Williams described and explained the mitral diastolic murmur in 1835 the aortic diastolic murmur and both aortic and mitral systolic murmurs had been widely recognized before this, in fact by Laennec himself In 1862 Austin Flint described his famous murmur of relative mitral stenosis without mitral cusp deformity In 1879 Roger reported the finding of his loud (grade 4 to 5) systolic murmur with palpable thrill just to the left of the sternum maximal in the third and fourth intercostal spaces in cases of congenital ventricular septal defect, sometimes called Roger's disease. The continuous murmur of a patent ductus arteriosus was described and explained by Fagge in 1873 In 1881 Graham Steell described the pulmonary diastolic murmur of high pressure in the pulmonary artery due to mitral stenosis as a rule, and named for Steell. Duroziez name is attached to the to-and-fro murmur heard over a large artery during pressure by a stethoscope in cases of free aortic regurgitation (1861) Gallop rhythm and its clinical importance were pointed out by Potain in 1875

Signs of heart failure have been recognized for many years and it was evident when the very first large collection of autopsies was made by Bonetus in 1679 that cardiac enlargement, both hypertrophy and dilatation, were important findings, sometimes attended by dyspnea, and indicative of strain although often unidentified as to type. Lancisi described in 1728 fullness and pulsation of the neck veins associated with right atrial and ventricular dilatation but many years, in fact nearly two centuries, went by before Mackenzie spread widely abroad this important sign of heart failure. When mediate auscultation came into common use a hundred years ago râles in the lungs, especially at the bases, became recognized as an evidence of pulmonary edema

due frequently to heart failure, but this sign has often been misjudged since so many other causes may be responsible. Dropsy that is, dependent edema, and liver enlargement were described by Bonetus in 1679 and recognized early as signs of heart disease and failure as well as being due to other diseases Munro published a treatise on dropsy in 1755

Pericarditis was one of the very first cardiovascular abnormalities noted and described, as seen in Benivenio s collection of autopsies in 1507 doubtless it was known to the ancients even though they did not recognize heart disease as such. Galen is said to have treated surgically an infected wound under the sternum which may have involved the pericardium. Effusions were well known to the compilers of postmortem data in the sixteenth and seventeenth centuries. Lower described cardiac tamponade in 1669 and Riolan (1653) followed later by Senac, too advised pericardial paracentesis, which was not done, however so far as records go until 1819 (Romero in Barcelona) Chronic pericardial scarring was an early discovery and the first *description of the special type called chronic constrictive pericarditis* was apparently given by Lower in 1669 but it was not presented as a clinical entity until 1842 when Chevers of Guy's Hospital in London described it. Wilks again referred to it in 1870 and finally in 1896 it was called Pick's disease after Pick who described "mediastinopericarditic pseudocirrhosis of the liver" Various minor signs have been attached to pericardial disease, Broadbent (1895) and Ewart (1896)—see Chapter 27 Surgery for chronic constrictive pericarditis was proposed by Delorme in 1898 but not carried out until 1913 (Sauerbruch) To date hundreds of cases have now been relieved by surgery

The recognition of the types of heart disease has been of the greatest importance of all advances in the entire field of heart disease as pointed out by Cabot's classical paper "The Four Common Types of Heart Disease," in the *Journal of the American Medical Association* in 1914 By the early 1920's the present-day fundamental classification of cardiac diagnosis based primarily on etiology had been independently introduced and well established at the Massachusetts General Hospital in Boston and at the Bellevue Hospital in New York City The major importance of this step was indicated not only by better diagnosis, prognosis, and treatment, but especially by directing attention to the causes of heart disease, the elucidation of which will doubtless lead to effective preventive medicine, so much more important in the final analysis than research, interesting though it is, in abnormal physiology and in therapy both medical and surgical.

Congenital heart disease, described in scattered reports by earlier workers, was first more adequately treated as such by Farre in 1814 and by Gintrac in 1824 Peacock's book on the subject in 1858 is much better known. Since then, progressive advances have been made in the works of Rokitansky (1875) Abbott (1908) Laubry and Pezzi (1921) and Taussig (1947) In 1938 the present era of spectacular cardiac surgery began with the first successful closure of a patent ductus arteriosus by Gross and Hubbard, al-

though Munro (1907) and others had suggested it and unsuccessful efforts had already taken place Since then other dramatic advances in surgical therapy have been made in congenital heart disease by Blalock and Taussig (1945) and by Potts (1946) in the alleviation of the tetralogy of Fallot, by Crafoord (1945) and by Gross (1945) independently in the cure of coarctation of the aorta, and by Gross (1945) in breaking a ring of the great vessels around trachea and esophagus. All these advances, dramatic and vital as they are, pale, however in comparison with the discovery by Gregg (1941) and Swan (1943) of Australia that congenital cardiovascular defects and cataracts are likely to be found at birth in babies born of mothers who had German measles (rubella) during the first two or three months of pregnancy

Rheumatic heart disease as an entity was first suggested by Pitcairn (1788) and Baillie (1793) although valvular defects had been well described pathologically since the days of Bonetus (1679) and earlier Bouillaud in 1840 established on a firmer footing the association between rheumatic fever and heart disease Aschoff discovered his more or less specific lesion in the myocardium in 1904 and in 1913 Poynton and Paine called attention to the importance of the hemolytic streptococcus as an exciting factor confirmed by Coburn in 1931 and by others since.

Subacute bacterial endocarditis was slowly separated from other heart troubles toward the end of the nineteenth century (Osler 1885) its causative agent, the Streptococcus viridans, was discovered by Schottmüller in 1910, and the disease was much studied by Libman (1910 and later) but it remained well nigh totally fatal until Loewe showed in 1944 that the majority of the cases can be cured by penicillin.

Cardiovascular syphilis was probably the first etiologic type recognized. Aortic aneurysms were attributed to syphilis by Paré about 1564 and aortic regurgitation with the cor bovinum was recognized as sometimes of syphilitic origin a hundred or more years ago. Reuter recognized aortitis as a syphilitic lesion in 1906 Intensive antisyphilitic treatment for aortitis has been developed effectively during the present generation, especially by Moore and his associates, at first with the heavy metals (1932) and recently with penicillin. The most important advance, however has been in preventive medicine through the early recognition and specific treatment of the chancre itself or by its prevention in the first place, resulting in an impressive drop, now in progress, in the development of aortic syphilis fifteen or twenty years after the original infection.

Other infections, bacterial and virus, and parasitic infestations of the heart and blood vessels involve relatively few individuals nowadays in contrast to their frequency often unrecognized as such, in days gone by before the control of these diseases became so impressive. Diphtheria, tuberculosis, influenza, and other virus diseases, trichiniasis and trypanosomiasis (Chagas, 1909 1922) have all been recognized and described by many workers, often lost in history but they are now of minor import. One might add, however

that the first actual proof of the influenza heart did not come until 1945 (Finland, et al.) In severe degree it is uncommon.

Thyroid disease as it involves the heart is now no longer a problem but thirty years ago thyrotoxicosis was recognized as an important though not common cause of heart disease. It was attacked successfully by surgery (subtotal thyroidectomy) by Lahey and Hamilton in 1923 The introduction of speedy surgical correction of thyrotoxicosis itself and of medical measures with iodine, thiouracil, and irradiated iodine has practically wiped out the thyrotoxic heart. The heart in myxedema was first clearly described in 1918 by Zondek it too is now very rare the disease itself having been brought largely under control.

The enlarged hypertensive heart was first described as an accompaniment of nephritis by Bright himself in 1836 In 1872 Gull and Sutton called attention to the arteriolar fibrosis found with these enlarged hearts. Both they and Bright considered that there must be present in these cases some special factor of strain, although hypertension had not yet been discovered. At the end of the nineteenth century blood pressure measurements in man began, and soon afterward hypertension was identified. It was considered as an entity separated from Bright's disease, and called hyperpiesia by Allbutt in 1895 The hypertensive heart had been serious when of high degree and not amenable to curative therapy until the advent of lumbodorsal sympathectomy (Smithwick, 1940) which has aided a large number of cases, demonstrating finally that every single type of heart disease may be reversible (White, 1944) The rice and low sodium diets have also helped some cases, but something better than any of these measures is needed to control the hypertension various drugs are now being hopefully investigated in this direction, especially the purified veratrum alkaloids, in particular protoveratrine.

The cor pulmonale (or pulmonary heart disease) has only very slowly come up for recognition. The chronic type has been known for several decades (associated particularly with silicosis, now under better control) but the acute cor pulmonale has only recently been described (McGinn and White, 1934)

The final of the more common or important types of heart disease, that due to coronary atherosclerosis, has already been referred to above in the writings of Heberden, Jenner and Herrick. It remains one of the chief problems of world health today and has, until the very present, been much neglected in research as to etiology and pathogenesis. Interesting clues have been recently uncovered, however and the future looks brighter

Other causes of heart disease have been recognized for generations but only lately has their incidence been more clearly analyzed. Cardiac and pericardial neoplasms have been noted on pathologic examination for centuries although at first there was great confusion in the diagnosis of the simple postmortem clots which, before Kerckring (1670) were called polyps and thought to indicate disease. In late years it has been possible even to make correct ante-

mortem diagnoses of neoplasm involving the heart and pericardium in a few cases. Traumatic lesions of the heart were also recognized very early but even today in nonfatal cases they comprise one of the most difficult, though fortunately uncommon, aspects of heart disease. Nutritional diseases involving the heart have become well recognized during the past generation, especially beriberi the acceptance of which has come slowly through the work of many different individuals. Somewhat similarly has been the elucidation of other rare cardiac involvement such as is discussed in Chapter 23 of this book including conditions like sarcoidosis, amyloid disease hemachromatosis, and lupus.

Finally a few words may be added about other therapy than that mentioned above concerning specific types of heart disease that is, in particular the treatment of myocardial and of coronary insufficiency and that of the arrhythmias. The two most important measures of treatment of myocardial and coronary insufficiency concern two medicines which have an interesting history *Digitalis* was the Latin word coined by Fuchs from the German *Fingerhut* when he introduced that plant (the foxglove) as an afterthought in his appendix to his great herbal in 1542. From that time on for nearly two and one half centuries, digitalis was officially used when it was given at all as an emetic, but in a family recipe for the dropsy it held an effective though obscure place, doubtless handed down for unnumbered years, until William Withering of Birmingham England, in 1775 happened to be enough interested in both the practice of medicine and botany to discover through a patient of his, its value in heart failure. For ten years he tested it before he published his small, but justly renowned, monograph on the foxglove in 1785 giving credit to Fuchs for its original introduction to medical botany More than another century elapsed, however before Withering's explicit and correct advice about dosage became current practice. During that century efforts were made to purify the crude drug and one hundred years ago Nativelle (1847) in France made digitoxin (digitaline Nativelle) which has very belatedly become popular in the U.S.A. Many preparations of digitalis are now available and effective meanwhile the dried leaves themselves remain a cheap and useful medicine too. In recent years there has been a tendency to give more of the drug both in distribution and in quantity than needed in contrast to its neglect for well over a century after Withering.

The second notable medicine is nitroglycerine (glyceryl trinitrate) invaluable in the treatment of periodic and frequently recurring coronary insufficiency in the form of angina pectoris. Preceded for a few years by amyl nitrite (Brunton, 1867) it was introduced by Murrell in 1879 to take the place of the much less effective and less practical employment of spirituous liquor originally suggested by Heberden himself in 1768 There is today no better measure. The most important advance in its use in recent years has been its employment prophylactically making more comfortable and safer the undertaking of certain necessary or unavoidable strains.

In the control of arrhythmias quinidine has already been mentioned. It was introduced by Frey in 1918 to control atrial fibrillation, four years after

a patient of Wenckebach had rediscovered the helpfulness of quinine referred to a century and a half earlier by Senac (1749) The other most important therapy of arrhythmia has been that of the effect of epinephrine parenterally in the control of Adams-Stokes attacks (Hardoy and Houssay 1917 Phear and Parkinson, 1922)

Many other drugs have, of course, been used in the treatment of heart disease from time immemorial, but brief mention may be added here simply of two. Mercury was employed centuries ago not only in the therapy of syphilis but also as a diuretic and, like bloodletting, for almost any disease in fact one poor girl with active rheumatic fever seriously ill at the Massachusetts General Hospital in 1846 was made miserable by the large doses of mercurial and many other drugs, the use of which was the custom of the day However it was not until Saxl in Vienna in 1920 accidentally discovered the more favorable effect of mercury given parenterally rather than by mouth that this currently important diuretic has come into its own. The other medicine which may be mentioned as an alleviator of misery though not a cure of heart disease, is salicylic acid and its salts, originally obtained from the bark of the swamp willow near the site where rheumatism itself was supposed to have been engendered. The salicylates have been used for generations to assuage the pains of acute rheumatic fever and, as a matter of fact, of other diseases such as rheumatoid arthritis for this purpose it has an essentially specific effect though the myocardial and endocardial manifestations of rheumatic fever are not appreciably helped. And now on the horizon there are appearing the important hormones, ACTH and cortisone, which give promise of controlling these diseases which involve the joints heart valves, and connective tissues.

In closing this chapter a comment may be added about the history of diet as it applies to heart disease. In general, apparently for centuries, advice has been given to individuals with cardiac symptoms and signs to eat lightly and of simple foods. Mackenzie, for example, in his volume on *Heart Disease* published in 1908 advised small meals of whatever easily digested foods the patient himself preferred. The two important advances that have come have both been rather recent first, the addition of vitamins as needed, especially when there is malnutrition often resulting from chronic heart failure on which occasion vitamin B complex and other vitamins (though not specifically vitamin E) have been helpfully added during the last generation. The much more significant advance, however has been the belated recognition of the importance of a low sodium intake in the presence, or under the threat, of congestive heart failure with accumulation of fluid in lungs, liver extremities, or elsewhere in the body A proper application of the helpful effect of a low sodium intake in the diet has been one of the great advances during the last decade. However the beginning of this dates back doubtless even before Karell in 1866 advised a very restricted milk diet consisting of only 800 cc of skimmed milk a day Almost certainly the chief value of this diet lay in the restricted sodium rather than in the restricted fluid intake. In 1903 Widal and Lemierre were the first clearly to show that it was the salt itself that was im-

portant. Allen in 1920 had used a low salt diet for hypertension and some of his cases with congestive failure were particularly benefited. It has, however been Barker in 1932, Schroeder in 1941 and Schemm in 1942 who presented convincing data of the effect of decreased intake of sodium in congestive heart failure One other diet may be mentioned because of its widespread use in the treatment of hypertension and that is the rice diet of Kempner (1944) This diet, low in protein and fat as well as in sodium has helped some patients with hypertension. The mechanism of its action has not been clarified. It is still under investigation.

In this chapter I have attempted briefly to present the trends of advance in our knowledge of cardiovascular disease, but we still have more to learn in our campaign to reduce the incidence of heart disease by preventive measures than we have already learned during all the ages that have gone before.

AN OUTLINE OF THE EVOLUTION OF OUR KNOWLEDGE OF THE HEART AND ITS DISEASES[1]

(Important contemporary events are to be found at the right side of the page in bold face type.)

B C

Imhotep (Egypt) 2980 B C. and successors. Observation of the pulse.

Hippocrates (Greece) 460 B.C. Treatises containing description and prognostic significance of symptoms and signs, including dyspnea and dropsy

Aristotle (Greece) 384 B C. Pulsation of the chick embryo s heart.

Erasistratus, Herophilus (Alexandria) 310 B.C. Anatomy of the human heart.

A.D

Celsus (Rome) earliest years of first century A.D *De Re Medicina*, including recommendation of venesection for severe dyspnea.

Dioscorides (Greek working in Rome) *De Medicinali Materia*, including the diuretic squill, 60 A.D

Galen (Greek working in Rome) 131 Detailed study of the pulse.

Hotel Dieu, Paris, 651
The Crusades
Medical School at Salerno, 1000
St. Bartholomew's Hospital, 1123
Bologna University 1156
Montpellier University 1180
Oxford University 1201
The Inquisition, thirteenth century
Magna Carta, 1215
Cambridge University 1223
Sorbonne University 1257
Al-Mansur Hospital at Cairo, 1283

1 A single asterisk indicates important entries, and double asterisks the more important entries in the historical table.

Ibn Nafis (Egypt) Pulmonary circulation, 1300

The Renaissance, fourteenth and fifteenth centuries
The Black Death, 1348
Invention of Printing, 1440

Leonardo da Vinci (Italy) 1452. Drawings of the heart.

Constantinople captured by the Turks, 1453
Martin Luther 1483–1546
Discovery of America, 1492

Benedetti (Italy) Case of malposition of the heart, 1493

HEART DISEASE NOT YET RECOGNIZED

1500

* **Benivenio** (Italy) *De Abditis Nonnullis ac Mirandis Morborum et Sanationum Causis* some of the earliest autopsy proof of the existence of heart disease including cases of endocarditis and fibrinous pericarditis, 1507

Berengario da Carpi (Italy) Commentary on the anatomy of Mondino (1516) with mention of a dilated heart, 1521

Botallo (Italian working in France) 1530 Description of the ductus arteriosus (Botalli)

Canano (Italy) Valves in veins, 1540

Mexico City Hospital, 1524

* **Vesalius** (Belgian working in Italy) *De Fabrica Humani Corporis* 1543 with description of human heart. Also antemortem recognition of aortic aneurysm, 1555 confirmed at autopsy two years later

Servetus (Spaniard working in France and Italy) Mention of the pulmonary circulation in his religious tract, *Restitutio Christianismi* 1553

Colombo (Italy) Description of the pulmonary circulation in *De Re Anatomica* 1559

Fernel } (France) Aortic aneurysm ascribed to syphilis. { *Medicina* 1554
Paré } { Surgery 1564

* **Caesalpino** (Italy) Introduction of term circulation with reference to movement of blood in arteries and veins, 1559

Schenck (Germany) *Observationum Medicarum Rarum* 1584 Important compilation of case records based on symptoms.

1600

Fabrizio d'Acquapendente (Italy) *De Venarum Ostiolis (Venous Valves)* 1603 Creation of the anatomical theater at Padua.

Albertini (Italy) *De Affectionibus Cordis* 1618 The first extensive treatise on the heart but with little important information largely a review of ancient and medieval theories with long discussion of palpitation and syncope.

The Thirty Years' War, 1618–1648

Aselli (Italy) Discovery of lacteal vessels, 1622

* Harvey (Englishman studying in Italy) *Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus* 1628 Proof of the circulation of the blood.

The Commonwealth (Cromwell) in England, 1649–1660

Pecquet (France) Description of the receptaculum chyli and thoracic duct, 1651

Bartholin (Denmark) Discovery of lymph vessels, 1653

Malpighi (Italy) *De Pulmonibus* containing a note on the discovery of capillaries, 1661

Plague in London, 1665
Great fire of London, 1666

Lower (England) *Tractatus de corde* 1669 This includes the experimental proof that dropsy may result from venous obstruction.

Kerckring (Holland) *Spicilegium anatomicum* 1670. Recognition that postmortem clots in the heart are not polyps or worms, their faulty interpretation had caused confusion for centuries.

* Mayow (England) *Tractatus duo* 1668, and *Tractatus quinque* 1674 Demonstration of the function of breathing to change venous blood to arterial blood by interchange of gases, the blood taking up the nitro-aerial spirit of the air in the lungs.

Stensen (Denmark) First description of the tetralogy of Fallot, 1672.

* Bonet (France) *Sepulchretum* 1679 Storehouse of case reports with autopsies, containing many instances of cardiovascular disease, such as that of the Parisian tailor who dropped dead in the street and showed post mortem a calcified stenosed aortic valve.

Siege of Vienna, 1683
Peter the Great (Russia), 1689–1725

1700

Cowper (England) Plate showing aortic stenosis, 1705

Floyer (England) *Physician's Pulse Watch* 1707 Recommendation of the recording of the pulse rate in health and disease.

Vieussens (France) *Traité du cœur* 1715 Description of coronary circulation. "Thebesian" vessels (Thebesius, 1716) and a few abnormalities of the heart, including mitral stenosis and dyspnea therefrom.

Albertini, Hippolito (Italy) Cardiac palpation as an aid to diagnosis, 1726

* **Lancisi** (Italy) *De Motu Cordis et Aneurysmatibus* 1728 Discussion of cardiac and aortic enlargement, and description of engorgement of neck veins with dilatation and failure of the right ventricle. Also *De Subitaneis Mortibus* 1707 The first treatise on sudden death, with autopsy findings in five cases.

* **Hales** (England) *Hæmastaticks* 1733 First study of blood pressure.

Senac (France) *Traité du cœur* 1749 Important textbook on the heart including observations on congenital defects and the use of quinine for rebellious palpitation.

Munro (England) Treatise on dropsy 1755

* **Morgagni** (Italy) *De Sedibus et Causis Morborum* 1761 Extensive discussion of pathology with many cardiovascular observations, including calcification of the coronary arteries.

Auenbrugger (Austria) *Inventum Novum*, 1761 Introduction of mediate percussion in the study of heart size and of pericardial and pleural effusions.

Heberden (England) Angina pectoris, 1768

Neubauer (Germany) Cardiac nerves, 1772.

Lavoisier (France) Respiratory gas exchange, 1777

Sandifort (Holland) Early description of tetralogy of Fallot, 1777

U.S.A., 1783

* **Withering** (England) *An Account of the Foxglove* 1785 Introduction of digitalis in the treatment of dropsy

Parry (England) Thyrotoxicosis and its effect on the heart, 1786.

Pitcairn (England) Rheumatism of the heart, 1788

French Revolution, 1789

Baillie (Scotland) *Morbid Anatomy* 1793 Description of endocarditis.

** **Jenner** (England) The relationship of angina pectoris to coronary disease, presented in a letter published by Parry in his *Syncope Anginosa* 1799

1800

Scarpa (Italy) Arteriosclerosis, 1804 He also gave an excellent description of the nerves of the heart in his *Tabulæ Nevrologicæ* in 1794

Corvisart (France) *Maladies du Cœur* 1806 Important textbook on the heart. He also restored Auenbrugger's percussion as an important method of examination, 1808

Burns (Scotland) Angina pectoris due to myocardial ischemia. Textbook on diseases of the heart, 1809

Wells (U.S.A.) Cardiac rheumatism, 1810.

* **Testa** (Italy) *Malattie del cuore* 1810.

Farre (England) Cardiac malformations including the tetralogy of Fallot, 1814

* Hodgson (England) *Treatise on the Diseases of Arteries and Veins* 1815

Kreysig (Germany) Textbook on heart diseases, 1815

* Cheyne (Ireland) First good description of Cheyne-Stokes breathing, 1818

* Laennec (France) *De l'Auscultation Médiate* 1819 Introduction of the stethoscope

Romero (Spain) Pericardial paracentesis 1819

Gintrac (France) Maladie bleue (morbus caeruleus) 1824

* Adams (Ireland) Classic description of the Adams-Stokes syndrome, 1827

Hodgkin (England) Aortic insufficiency 1827

Andral (France) Pulmonary arteriosclerosis, 1829

* Hope (England) *A Treatise on Diseases of the Heart and Great Vessels* 1832, containing a description of left ventricular failure with pulmonary vascular congestion and cardiac asthma.

* Corrigan (Ireland) Aortic insufficiency 1832. The Corrigan pulse.

Lobstein (France) Arteriosclerosis, 1833

Williams, C J B (England) *The Pathology and Diagnosis of Diseases of the Chest* 3rd edition, 1835 Description of the mitral diastolic murmur among other murmurs.

Bouillaud (France) *New Researches on Acute Articular Rheumatism* (with its relationship to acute and chronic endocarditis and pericarditis) 1836

* Bright (England) Association of heart disease with kidney disease, 1836.

Magnus (Germany) Respiratory function of the blood, 1837

Skoda (Austria) Treatise on percussion and auscultation, 1839

Purkinje (Bohemia) End branches of the atrioventricular bundle—the Purkinje fibers, 1839 He also described the visual toxic effects of digitalis.

Chevers (England) Description of chronic constrictive pericarditis, 1842.

* Hall (England) Sudden death due to arrest of coronary circulation, 1842.

Weber Brothers (Germany) Vagal inhibition of the heart, 1845

Nativelle (France) Introduction of digitoxin (digitaline) 1845

Hutchinson (England) Introduction of the determination of the vital capacity of the lungs, 1846

Ludwig (Germany) Introduction of the graphic method, 1847

1850

Bernard (France) Vasomotor nerves, 1851

Stannius (Germany) Heart block, 1852.

Kirkes (England) Peripheral embolism from valvular vegetations, 1852.

Stokes (Ireland) Textbook od heart disease, 1854

* Kölliker and Müller (Germany) Cardiac electricity 1855
* Vierordt (Germany) Sphygmography introduced, 1855
Virchow (Germany) Thrombosis and embolism 1856
Peacock (England) *Malformations of the Heart* 1858
Foster (England) Rhythmicity of the heart, 1859
Marey (France) Sphygmograph, 1860
Duroziez (France) Vascular murmurs of free aortic regurgitation, 1861
Flint (U.S.A.) The murmur of relative mitral stenosis, 1862.
Raynaud (France) Vasoconstriction in the hands, 1862.
Karell (Russia) Restricted diet in heart failure, 1866
Kussmaul (Germany) Periarteritis nodosa, 1866 Pulsus paradoxus, 1873
Brunton (England) Amyl nitrite introduced for angina pectoris, 1867
* Fick (Germany) Blood flow studies, 1870
Da Costa (U.S.A.) Irritable heart of soldiers, 1871
Traube (Germany) Description of alternation of the pulse and of cardiorenal disease 1872.
Gull and Sutton (England) Arteriocapillary fibrosis, 1872.
Welch, F H. (England) Differentiation of aortic syphilis from aortic atheroma, 1875
Rokitansky (Austria) Septal defects, 1875
Southey (England) Tubes for anasarca, 1877
Welch, W H. (U.S.A. studying in Germany) Acute pulmonary edema, 1878
Sanderson and Page (England) Study of heart action by capillary electrometer 1878
Rosenbach (Germany) Cardiac reserve 1878
Roger (France) Murmur of interventricular septal defect, 1879
Murrell (England) Nitroglycerine introduced in treatment of angina pectoris, 1879
Winiwarter (Germany) Endarteritis, 1879
Barié (France) Traumatic lesions of the heart valves, 1880.
* von Basch (Germany) Introduction of the sphygmomanometer 1881
Gaskell (England) Heart block, 1881
Steell (England) Murmur of functional pulmonary regurgitation, 1881
Concato (Italy) Polyserositis, 1881
Leyden (Germany) Coronary artery disease 1884
Osler (Canada, U.S.A. and England) Bacterial endocarditis, 1885
Waller (England) Human electrocardiography 1887
Bristowe (England) Paroxysms of tachycardia, 1887
Fallot (France) Congenital heart disease—Fallot's tetralogy 1888
Bouveret (France) Paroxysmal tachycardia, 1889
Riva-Rocci (Italy) Development of sphygmomanometer 1891
Kent (England) } Atrioventricular bundle, 1893
His (Germany) }
Bayliss and Starling (England) Electrocardiographic studies, 1893

Einthoven and Geluk (Holland) Phonocardiography 1894
Allbutt (England) Hyperpiesia, 1895
Broadbent (England) Pericarditis, 1895
Ewart (England) Signs of pericardial effusion 1896
Porter (U.S.A.) Coronary circulation 1896
* **Marie** (France) Myocardial infarction 1896
Farina (Italy) and Rehn (Germany) Operations on the heart, 1896
Pick (Germany) Chronic mediastinopericarditic pseudocirrhosis of the liver 1896. Chronic constrictive pericarditis first described by Chevers in 1842.
Williams (U.S.A.) Roentgen ray study of the heart, 1896 Roentgen introduced the new ray in 1895
Delorme (France) Pericardial resection suggested, 1898
Gibson (Scotland) Textbook on heart disease, 1898
Fiedler (Germany) Interstitial myocarditis, 1899

1900

Mackenzie (Scotsman working in England) *The Study of the Pulse* 1902
* Moritz (Germany) Orthodiagraphy of the heart, 1902.
Brauer (Germany) Precordial rib resection, 1902.
Carrel (Frenchman working in U.S.A.) Arterial suture 1902.
Matas (U.S.A.) Aneurysmorrhaphy 1902.
* **Einthoven** (Holland) Introduction of the string galvanometer for electrocardiography 1903
* **Wenckebach** (Hollander working in Germany and Austria) Arrhythmia of the heart, 1903
Widal and Lemierre (France) Low sodium intake for congestion, 1903.
* **Aschoff** (Germany) Myocardial lesions in rheumatic fever 1904
Pal (Austria) Vascular crises, 1905
* **Köhler** (Germany). Teleroentgenography 1905
Korotkow (Russia) Auscultatory sphygmomanometry 1905
Romberg (Germany) Textbook on heart disease, 1906.
Reuter (Germany) Demonstration of spirochaeta pallidum in aorta in syphilitic aortitis, 1906
Keith and Flack (England) Discovery of the sinoatrial node 1907
Tawara (Japanese working in Germany) The atrioventricular node and its connection with the bundle, its branches, and the network of Purkinje fibers, 1908
Buerger (U.S.A.) Thromboangiitis obliterans, 1908
Abbott (Canada) Congenital defects, 1908
Trendelenburg (Germany) Pulmonary embolectomy 1908
Pachon (France) Oscillometry 1909
* **Rothberger and Winterberg** (Austria) Atrial fibrillation recognized clinically 1909

* **Lewis** (Welshman working in England) Atrial fibrillation recognized clinically- independent observation, 1909 Blood vessels of the skin, 1927

Schottmüller (Germany) Identification of the Streptococcus viridans as the cause of subacute bacterial endocarditis, 1910

* **Lian** (France) Left and right-sided heart failure, 1910

Hirschfelder (U.S.A.) Textbook on heart disease, 1910

Libman (U.S.A.) Subacute bacterial endocarditis, 1910

Ritchie (Scotland) Atrial flutter 1911

Herrick (U.S.A.) Clinical recognition of coronary thrombosis, 1912.

Anitschkow (Russia) Atherosclerosis, 1912.

Krogh and Lindhard (Denmark) Blood flow 1912.

Sauerbruch (Germany) Pericardial resection, 1913

Cabot (U.S.A.) Etiology of heart disease, 1914

World War I, 1914–1918

Cohn (U.S.A) Digitalis effect on *T* wave of the electrocardiogram, 1915

Eggleston (U.S.A.) Digitalis dosage, 1915

Jonnesco (Roumania) Sympathectomy for angina pectoris, 1916

Oppenheimer et al. (U S.A.) Neurocirculatory asthenia, 1918

Smith (U.S.A.) Coronary electrocardiogram, 1918

Levine and Tranter (U S.A.) Myocardial infarction, 1918.

Frey (Germany) Introduction of quinidine in the treatment of atrial fibrillation, 1918

Zondek (Germany) The heart in myxedema, 1918

Christian (U S A.) Digitalis in normal rhythm, 1919

Pratt (U S.A) Digitalis strength, 1919

Wyckoff (U S A.) Classification of cardiac diagnosis, 1919

Specialization

Pardee (U.S.A.) Coronary *T* waves of the electrocardiogram, 1920

Saxl (Austria) Mercurial diuretic injections, 1920

Rehn (Germany) Pericardial resection, 1920

Reid (U.S.A.) Effect of arteriovenous fistula on heart, 1920

Gross (Canada) Coronary artery injections, 1921

Vaquez (France) Textbook on heart disease, 1921

White and Myers (U.S A.) Classification of cardiac diagnosis, 1921

Krogh (Denmark) Capillary physiology 1922.

Key (Sweden) Embolectomy 1922.

Chagas (Brazil) Cardiac trypanosomiasis, 1922 (1909)

Scott (U.S.A.) Quinidine for ventricular paroxysmal tachycardia, 1922.

Plummer (U.S.A.) Iodine in the initial treatment of thyrotoxicosis, 1923

Hering (Germany) Carotid sinus reflex, 1923

American Heart Association established, 1924

Hamilton and Lahey (U.S.A.) Cure of thyrocardiacs by subtotal thyroidectomy (the first clear demonstration of the reversibility of heart disease) 1924
Schmieden (Germany) Pericardial resection, 1924
Cutler (U.S.A.) Valvulotomy 1924
Parkinson (England) Epinephrine in Adams Stokes attacks, 1924
Rowntree and Adson (U.S.A.) Bilateral lumbar sympathectomy for hypertension 1925
Mandl (Austria) Paravertebral nerve injection for angina pectoris, 192
Cannon (U.S.A.) Accessory cardiac nerves. Discovery of sympathin from the thoracic sympathetic chain, 1926
Blumgart and Weiss (U.S.A.) Velocity of blood flow 1927
Wenckebach and Aalsmeer (Holland) Beriberi heart, 1928
* Keefer and Resnick (U.S.A.) Angina pectoris, 1928
Keith, et al. (U.S.A.) Malignant hypertension, 1928
Weber (Czechoslovakia) Electrocardiogram in familial periodic paralysis associated with potassium lack, 1928
Erdheim (Austria) Medionecrosis aortae idiopathica, 1929
von Gierke (Germany) Glycogenic visceral enlargement, 1929
Forssmann (Germany) Cardiac catheterization, 1929 angiocardiography 1931
Edens (Germany) Textbook on heart disease, 1929
Churchill (U.S.A.) Pericardial resection, 1929
Laubry (France) Textbook on heart disease, 1930
Wilson (U.S.A.) Bundle branch block, 1930 Direct and chest leads in electrocardiography 1930–1936
Grant (Scotsman working in England) Arteriovenous anastomoses, 1930.
Coburn (U.S.A.) Hemolytic streptococcus infection and rheumatic fever 1931
Wood and Wolferth (U.S.A.) Precordial leads in coronary occlusion, 1932.
Manca (Italy) Virus myocarditis (mumps) 1932.
Blumgart, Levine, and Berlin (U.S.A.) Total thyroidectomy for angina pectoris and heart failure, 1933
Goldblatt (U.S.A.) Hypertension produced by renal ischemia, 1934
Shennan (England) Dissecting aortic aneurysms, 1934
Leary (U.S.A.) Coronary atherosclerosis, 1935
Beck (U.S.A.) Pericardial implantation of pectoral muscle to bring new blood vessels to the heart seriously affected by coronary disease 1935
McGinn and White (U.S.A.) Acute cor pulmonale, 1935
Castellanos (Cuba) Angiocardiography in disease, 1937 Robb and Steinberg (U.S.A.) 1938.
Schlesinger and Blumgart (U.S.A.) Coronary occlusions and collateral circulation, 1937–1941

Winkler Hoff, and Smith (U.S.A.) Electrocardiograms in potassium poisoning (including uremia) 1938 1941 Chamberlain, et al., 1939 Keith, et al., 1942.

Taussig (U.S.A.) Tricuspid atresia, 1938

Gross and Hubbard (U.S.A.) Successful ligation of patent ductus arteriosus, 1939

Smithwick (U.S.A.) Radical splanchnic resection for hypertension, 1940 (Development of Peet's operation, 1935)

Mannheimer (Switzerland) Calibrated phonocardiography 1939

World War II, 1939–1945

Link, et al. (U.S.A.) Dicumarol as anticoagulant, 1940

Hahn (U.S.A.) Blood volume determined by radioactive iron, 1940

Gregg, Swan (Australia) Congenital defects due to rubella in pregnancy 1941–1943

Hubbard (U.S.A.) Excessive tachycardia in young infants as a cause of marked cardiac enlargement, 1941

Rappaport and Sprague (U.S.A.) Phonocardiography 1941–1942.

Cournand, Richards, et al. (U.S.A.) Cardiac catheterization and determination of right heart blood pressure, 1941 1944 McMichael (England) 1944

Kempner (U.S.A.) Rice diet for hypertension, 1944

Aub et al. (U.S.A.) Bacterial toxic factor in shock, 1944

Elkin (U.S.A.) Arteriovenous fistulae and their surgical correction, 1944

Chavez (Mexico) National Institute of Cardiology Mexico, 1944

* Loewe (U.S.A.) Cure of subacute bacterial endocarditis by penicillin, 1944

White (U.S.A.) Reversibility of heart disease, 1944

Henny Boone, and Chamberlain (U.S.A.) Electrokymography 1945

Finland, et al. (U.S.A.) Influenzal virus myocarditis, 1945

Blakemore, Lord, and Whipple (U.S.A.) Portal hypertension and porta venal shunts for relief thereof 1945

Blalock and Taussig (U.S.A.) Operation for tetralogy of Fallot, 1945 (Potts, 1946)

Crafoord (Sweden) Operation for coarctation of aorta, 1945

Gross (U.S.A.) Operation for coarctation of aorta, 1945 surgical relief for tracheal obstruction from a vascular ring, 1945

Lenegre (France)
Hecht (U.S.A.) } Intracardiac electrocardiograms, 1946.

Dexter (U.S.A.) Determination of pulmonary blood pressure, 1946.

Taussig (U.S.A.) Congenital heart disease, 1947

National Heart Institute, U.S.P.H.S., 1948

Blumgart, et al. (U.S.A.) Radioactive iodine therapy of refractory coronary and myocardial insufficiency 1948

Bland and Sweet (U S.A.) Venous shunt for mitral stenosis, 1948
Brock (England) Surgery for pulmonary stenosis, 1948
Murray (Canada) Repair of ventricular and atrial septal defects, 1948.
Krayer (U.S.A.) Protoveratrine in hypertension, 1949
Hench, et al (U S.A.) ACTH in rheumatism, 1949
Bailey, Harken } U.S.A. Operations on mitral valve for stenosis thereof 1949–1950

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Corvisart, J N *Essai sur les Maladies et les Lésions organiques du Coeur et les gros Vaisseaux* Migneret, Paris, 1806
Garrison, F H *An Introduction to the History of Medicine* W B. Saunders Co., Philadelphia, 4th ed., 1929
Herrick, J B. *A Short History of Cardiology* Charles C. Thomas, Springfield, Ill., 1942.
Hope, J A. *Treatise on the Diseases of the Heart and Great Vessels.* William Kidd, London, 183_.
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Osler W *The Evolution of Modern Medicine* Yale University Press, New Haven, 1923.
Senac, J B *Traité de la structure du coeur de son action, et de ses maladies.* Briasson, Paris, 1749
Vieussens, R. *Traité Nouveau de la Structure et des Causes du Mouvement naturel du Coeur* Jean Guillemotte, Toulouse, 1715
White, P D "The Reversibility of Heart Disease. *Illinois M J* 1944 LXXXVI, 9
"Cardiology as Specialty *Am. Heart J* 194_, XXIII, 161

PART I

CARDIOVASCULAR EXAMINATION
SYMPTOMS and SIGNS

CHAPTER 2

THE RANGE OF THE NORMAL HEART

Six years have elapsed since this chapter was written as useful introduction to this volume; few changes in it have been necessary since in this interval of time little has been added to our knowledge of the range of the normal heart, despite the great interest and importance of the subject occasioned by the examination f many hundreds of thousands of healthy young men for military service.

"It is requisite that every intelligent Patient should try his Pulse in a Morning in his Health, that he may inform his Physician what number of Pulses he has in a perfect Health, by which a Physician may judge of his natural Constitution and the Physician may know how far the diseas d Pulse recedes from the natural Numbers, nd whether the Numbers of the Pulse are increas d or be deficient, by which he may discern whether 'tis a hot or a cold disease so wrote Sir John Floyer in 1707 in the *Pulse Watch*.

The words I have just quoted make up one of the rare examples in medical literature, old or new not only of the recognition of the wide range of bodily measurements and functions of humankind in health, but, what is still more important, also of a relatively simple and accurate method of determining changes denoting abnormality in any given individual, thus avoiding the many clumsy and inaccurate measures that have been devised for general use.

The range of the normal heart remains today in cardiovascular physiology one of the most difficult problems accurately to assess, and in the diagnosis of cardiovascular disease one of the most important and yet neglected subjects. It is astonishing to find relatively so little written about it in works on medicine by either ancient or modern authors. As a matter of fact, the ancients actually paid more attention to the problem than have the moderns, largely without doubt because they had to do so since they didn't even recognize the existence of heart disease. Galen, Avicenna, and other authorities of the classical and medieval ages tried, for example, in their analysis of the pulse, which is as *far as they got in cardiology* to explain all variations on the basis of age, sex, temperaments (hot, cold, moist, and dry) seasons of the year climate, locality food and drink, sleep and waking, athletic exercise,

pregnancy pain, disease elsewhere in the body and emotional states (anger delight, joy grief and fear) Under the circumstances they did an extraordinarily good job in showing how all of these conditions may affect the pulse many of us today might profitably take a leaf from their book.

In the sixteenth century the pendulum began to swing back a little when autopsies revealed, through the findings of chronic heart lesions, the fact that the heart could be diseased and yet life continue. Gradually as more and more evidence of the frequency and multiplicity of heart disease was discovered, the impetus of the backswing of the pendulum accelerated through the centuries until it reached its maximum (we hope) early in the nineteenth century with such authorities as Corvisart, Napoleon s physician. He asserted that heart disease was, with the single exception of pulmonary tuberculosis, one hundred times the most common of all organic diseases in France, both in public and in private practice. He thought the majority of cases of asthma, hydrothorax, and various other conditions were the result of heart disease and that cardiac fatalities were very likely more numerous than deaths due to lesions of brain, stomach, liver kidneys, and other organs combined. He even scorned the idea of the need of statistical proof for these remarks. He attributed the frequency of heart disease to the hard or rather constant work of the heart and to the passions of mankind.

Just thirty years later however in 1836 John C. Williams of Edinburgh wrote a book on "Practical Observations on Nervous and Sympathetic Palpitation of the Heart, Particularly as Distinguished from Palpitation the Result of Organic Disease (Figure 1) He deplored the frequency with which functional derangement of the heart was attributed to heart disease itself and brought the pendulum a wee bit back from the extreme swing, the reverse of Galen s, for which Corvisart and others of that day and since were responsible. He wrote that *palpitation* was

"frequently by a careless observer regarded as symptomatic of some serious organic or structural change being established, either in the coverings of the heart, its muscular texture, or in some of its valvular appurtenances. A careful and deliberate inquiry however he went on to say "will, in the generality of cases, enable us to strip them of their apparent obscurity and danger and reduce them to their true place in nosological arrangement. Latterly there has been too great a rage for tracing diseases almost exclusively to *vascular* derangement. I deprecate this, because I am convinced of the unceasing influence of the nervous system, both in health and in disease. A deservedly popular writer on medicine of the present day says, 'The longer we live, the more we see and the deeper we study so much the more shall we become convinced, that not only are the primary impressions of morbific causes sustained by the sentient system of the human fabric, but it is here the primary morbid movements first begin, and are thence propagated to the vascular apparatus, which from that moment re-acts upon, and is again influenced by the nervous system. No man, I am satisfied, can ever be a sound Pathologist, or a judicious practitioner who devotes his attention to one of these systems in preference or to the exclusion of the other through life they are perpetually acting, and inseparably linked, together

PRACTICAL OBSERVATIONS

ON

NERVOUS AND SYMPATHETIC

PALPITATION OF THE HEART,

PARTICULARLY AS DISTINGUISHED FROM

PALPITATION

THE RESULT OF ORGANIC DISEASE

TO WHICH ARE PREFIXED SOME GENERAL REMARKS ON THE

USE OF THE STETHOSCOPE,

A

EMPLOYMENT OF PERCUSSION

IN DIAGNOSIS OF DISEASES OF

THE HEART AND LUNGS.

BY JOHN CALTHROP WILLIAMS M D

[illegible]

PHYSIC[illegible] TO THE NOTTINGHAM DISPENSAR[illegible] TO TH[illegible] [illegible]TTING[illegible] AN[illegible]
UNION [illegible] L AN[illegible] [illegible]PENSARY; LECTU[illegible]ER ON TH[illegible] PRINCIPLES
AN[illegible] PRACTICE OF [illegible]; EXTR[illegible] [illegible] ME[illegible]ER [illegible] THE
[illegible]AL MEDICAL SOCIETY EDINBURGH
&c.

Quo quis rectius cognoscit morbum, eo rectius sanat.

——— Si quid novisti rectius istis,
Candidus imperti; [illegible] non, his utere mecum. —Hor.

LONDON:

LONGMAN REES, ORME, BROWNE, AND CO. PATERNOSTER ROW

NOTTINGHAM: J. DICKLIN JOURNAL OFFICE.

1836.

FIG. 1 Title page of book by John C. Williams, 1836, on nervous and sympathetic palpitation of the heart.

Williams also quoted "the late eminent Dr Baillie" as follows

"There are in truth few phenomena, which puzzle, perplex, and lead into error the inexperienced (and sometimes the experienced) practitioner so much as inordinate action of the heart. He sees, or thinks he sees, some terrible cause for this tumult in the central organ of the circulation, and frames his portentous diagnosis and prognosis accordingly In the pride of his penetration he renders miserable for the time the friends—and by his direful countenance damps the spirits of his patient. But ultimate recovery not seldom *disappoints* his fears, and the Physician is mortified at his own success."

Finally Williams presented several case reports, the most striking of which was that described by Morgagni of a boarding mistress who had palpitation. She was bled with some appearance of relief The palpitation returned and so she was bled again daily until she died. Nothing abnormal was found at autopsy in thorax or abdomen, and Morgagni wrote,

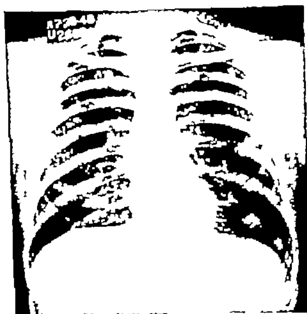
It would have been well had her physician remembered, that the very name of Palpitatio Cardiaca implies a course of proceeding quite the reverse

Like the rest of the body the heart varies in size and shape and action from one person to another somewhat according to sex and age and body size. Even when we take into careful consideration these three factors, however the range of the normal heart is too wide for us to know whether or not there has been some slight enlargement from strain or infection or otherwise, or some slight change in shape, or a change in action in almost any given case. This is true even of postmortem measurements of weight and volume and shape, and all the more so of clinical findings by physical examination, or by x ray electrocardiographic, and physiologic measurements of the circulation (Figure 2) I do not mean that this difficulty should prevent us from constructing and utilizing tables based on our present knowledge, but we should clearly recognize their inadequacy and seek better correlative factors than we have at our disposition to date Body build, aside from size, largely a family inheritance, is unquestionably of great importance and yet we have largely neglected it. Other bodily measurements besides height and weight and surface area need evaluation. We have found, for example, that the hearts of identical twins resemble each other closely on physical examination and by x-ray study and electrocardiography although it is still possible to distinguish by minor details the electrocardiogram of one twin from that of the other

Moreover in a given person one must use great judgment in comparing the findings from day to day or hour to hour based on clinical examination. The height of the diaphragm is of the greatest importance especially in the analysis of x-ray films and electrocardiograms (Figures 3 4 and 5) It changes constantly not only with ordinary breathing but with the amount of food or air in the stomach, the bulk of the contents, solid or gaseous, of the intestines, the enlarging uterus in pregnancy the addition of fat which is so



A



B

FIG. 2. A comparison of the appearance of the heart shadows in roentgenograms of two individuals without heart disease who died noncardiac deaths and who showed at autopsy heart weights of 700 grams each without any evidence of cardiovascular abnormalities.

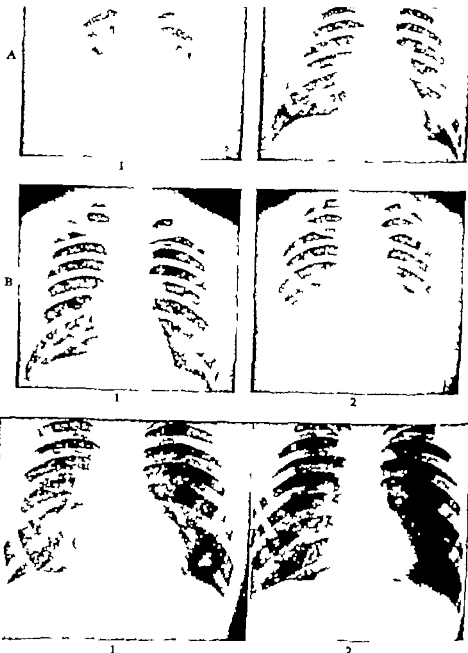


FIG. 3 Roentgenograms of the thoraces of normal young men showing the effects on *the heart shadows of alteration of the level of the diaphragm in respiration.* (*A*) Short stocky physician (1) during quiet breathing in upright position (2) at height of full inspiration in upright position. (*B*) Slender young physician (1) during quiet breathing in upright position, (2) at height of full expiration in upright position. Note the similarity f *A*1 and *B*2 and of *A*2 and *B*1

(*C*) B.W mal ge 27 (1) Normal control deep inspiration, immediate exposure; T.D 14.6 cm, height f diaphragm, 13 1 cm. (2) Effect of Valsalva's experiment deep inspiration, followed by forced expiration against 40 mm Hg for 5 seconds; T.D 1.2 cm, height of diaphragm, 12.4 cm. T.D = transverse *diameter* f heart.

often deposited in the abdomen or in its wall, certain intra-abdominal diseases particularly resulting in enlargement of liver or spleen, ovarian cyst, or ascites, diaphragmatic herniation, and, finally with certain intrathoracic diseases, especially those that cause an extreme pulmonary emphysema, with deep lowering and little motion of the diaphragm. It is often not realized that the prolonged fixation of the diaphragm at the level of full held inspiration (simulating the Valsalva experiment) results in an appreciable decrease in the size of the x-ray heart shadow (Figure 3C) this can result in erroneous estima-

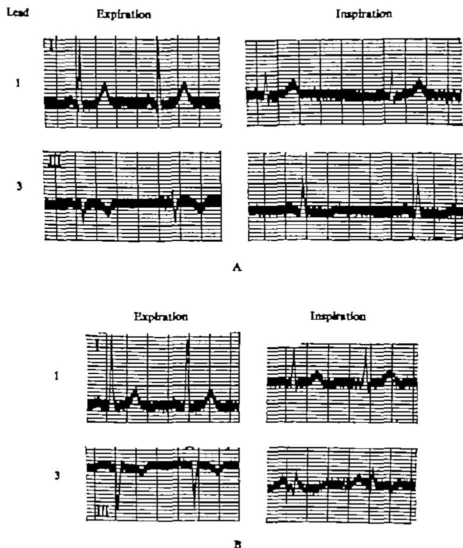


FIG. 4 Electrocardiograms (Leads 1 and 3) from two normal individuals, (*A*) and (*B*) showing the effect of deep expiration and inspiration on the deviation of the electrical axis.

tion of heart size if roentgen studies of the lungs are used for cardiac appraisal (see Chapter 7)

Besides the height of the diaphragm, the position of the body itself makes a difference (Figure 6) One should always stipulate, therefore whether an examination physical, x-ray or electrocardiographic is made in the upright position or recumbent. In our own cardiographic laboratory years ago we

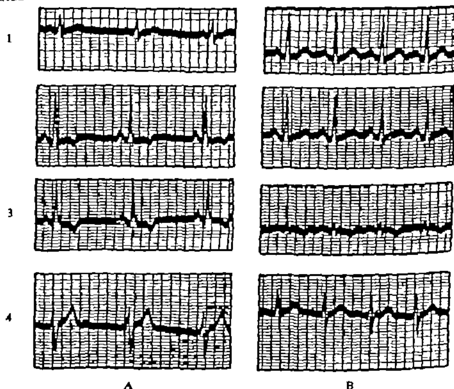
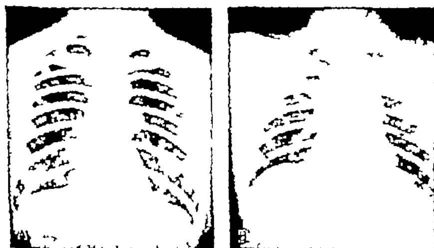


FIG. 5 Electrocardiographic changes (4 leads) with respiration in normal healthy man of stocky build. (*A*) At height of full inspiration. (*B*) At height of full expiration. Lead 4 was taken with exploring electrode over the fifth intercostal space at the left midclavicular line and the remote electrode on the left leg. (Graybiel and White, *Electrocardiography in Practice* W B. Saunders Company Philadelphia, 1941 Figures 16 and 17)

didn't record the position, although the tracings were almost always made with the patient sitting comfortably In the last ten years, however since we found what a difference position may (though it usually does not) make, we have recorded by a simple straight line the angle of the patient's body Positions of diaphragm and of body influence not only the anatomic and electric angle of the heart in the frontal plane but result in a rotation which is also important in its effects, though not so easy to measure.

The immediate state of health is another vital factor frequently influencing the heart findings on examination. A heart perfectly normal to start with,

and even later on showing normal myocardium endocardium, valves, and pericardium at autopsy may dilate acutely or subacutely from the effect of severe hypochromic anemia, massive pulmonary embolism (to produce the acute cor pulmonale) and paroxysmal tachycardia at excessive rates, as, for example, in the case of infants, where the heart rate may reach 300 or more a minute and result not only in general cardiac dilatation but also in congestive failure with engorgement of the liver Some of these infants have been erroneously diagnosed as having the so-called idiopathic hypertrophy of the heart, and some have been wrongly regarded as abdominal emergency



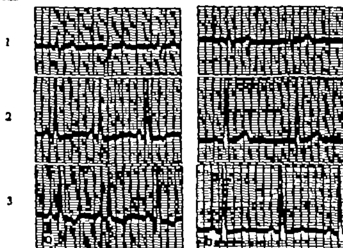


FIG. 6. Roentgenograms of the thorax of healthy young man (above) and electrocardiograms (limb leads) of another healthy young man (below) both slender in build, showing the effect of change in body (and heart) position—(*A* and) sitting upright, (*B* and *b*) lying supine.

cases, for example, pyloric stenosis, because of the vomiting caused by the acute congestive failure. Severe infectious diseases may also alter the presumably normal cardiac findings on examination without producing actual heart disease. Acute rheumatic infection can of course, precipitate acute or subacute cardiac dilatation and failure from the rheumatic myocardial disease, and diphtheria may seriously affect the myocardium, but, leaving these two specific infections out, there are still other infections like pneumonia which may cause temporary systolic murmurs, and even electrocardiographic changes, especially in rapidly growing or delicate individuals. Whether these murmurs are to be ascribed always to slight dilatation or how much the speeding up of blood flow has to do with them we don t know It is clear, however that thyrotoxicosis, without producing actual heart disease in the acute cases can alter the findings on examination of the heart, not only in producing a tachycardia and increased pulse pressure, but by the increased pulmonary blood flow causing marked accentuation of a physiologic pulmonary systolic murmur and a bulging of the pulmonary arc in the x-ray picture simulating a mitral shape of heart shadow

How much the factor of physical strain is responsible for changes in heart size and shape in man we don't know Once upon a time the medical profession as well as the laity talked glibly of the athletic heart. When most "athletic hearts" were shown to be something else, the term went into the discard, and now we doctors say almost as glibly that there is no such thing as an athletic heart. However a revision of the past and present opinions is still awaited on the basis of most careful studies not yet adequately assembled. There is a hint from several sources, including an annual appraisal of Harvard oarsmen which was for some years conducted by various associates of mine, that an occasional, or more likely a rare, person may after some years of excessively strenuous sport, develop an increase in heart size out of keeping with any increase in body size. This sort of change is reasonable to expect in view of experimental evidence in animals, where it has been shown that long-continued physical exercise produces hearts that are distinctly larger than those of animals kept very quiet, and in view of the well-known fact that hares have relatively very much larger hearts than have rabbits, racing greyhounds than other dogs, and race horses than ordinary mounts. Exercise can, of course, produce transient systolic murmurs, mostly in the pulmonic area, or increase those already present, even in normal persons. Another point of interest is that a trained athlete tends to have a slow pulse or one that slows quickly after exercise, although I can well remember counting the pulse rate of the winner of a marathon race a few years ago and finding it faster (118) at the starting line before he had taken a step than at the finish (110) after running 26 miles in his case nervous tension as to the outcome of the race was doubtless responsible, acting like stage fright. I would hasten to add, however *that there is no evidence that vigorous exercise in* the case of a healthy person in good training hurts the heart. If anything, the reverse is true as pointed out by Morgan in a volume entitled *University Oars* published by

Macmillan in London in 1873 In this book data are presented which indicate that the Cambridge and Oxford oarsmen of a hundred years or more ago outlived their expectation. It may well be that the change to a very sedentary life is more harmful than a maintenance of exercise.

The effect of high altitude on the heart and circulation is in rare individuals an important consideration. Not many persons have exposed themselves to altitudes of 12,000 feet or more as permanent residents, or even temporarily but now of course with the circulatory adjustments in aviators, especially in military service, the problem has become acute. Circulatory collapse probably antedates serious cardiac involvement itself in mountain climbers and in aviators, in the latter either from the effect of low oxygen tension in the atmosphere or from the centrifugal force of great speed and change in direction, or from still other factors. Residents at very high altitudes do however show circulatory adjustments that have been well described and resemble somewhat those in the cyanotic type of congenital heart disease at sea level. Tandler has pointed out incidentally that the bird Lagopus living in the Alps has a heart weight 50 per cent greater than that of the Lagopus of the same size living at lower altitudes.

The factor of the effect of rapid growth on cardiac findings has not yet been completely assessed. It is the impression of many of us that a fast-growing boy or girl, or indeed a delicate child of any age, is very prone to show an instability of circulation and heart action, and easily induced heart murmurs, from fatigue, overexertion, or mild infection, that do not signify the presence of heart disease or active rheumatism which we are so prone to suspect in our climate in New England, and rightly so of course, in many cases. We need more enlightenment in this problem.

I have already referred to pregnancy as a factor which alters the height of the diaphragm and so affects both x-ray picture of the heart and electrocardiogram, but it has other results too Through the influence of the increased blood volume and circulation, the heart volume is itself somewhat increased, and pulmonary and even apical and aortic systolic murmurs may appear due in part to such factors and in part to the upward displacement of the heart and great vessels.

Still further factors significantly affecting the action of the normal heart are the emotions, as pointed out by the ancients and restated by Williams. Not only may fear and pain alter heart rate, blood pressure, heart sounds, and subjective sensations, but through action on the sympathetic and parasympathetic nerves they may even alter the electrocardiogram. With tachycardia the *T* waves are often depressed and on occasion excessively so even inversion of the *T* waves has been induced by sudden fright, as it has been also, but doubtless through a different mechanism, by drinking ice water

And finally we come to the toxic influences of drugs or poisons on the normal heart. Those that are best known are the effects of digitalis, atropine, and quinidine, but there are doubtless less well-known drug actions or the influence of rare poisons that need exploration. This is an important digres-

sion, for toxic effects on an otherwise normal heart may simulate serious disease as was so well borne out in the famous insurance racket in New York City some years ago, when a few crooked doctors, lawyers, and insurance clients conspired to defraud the companies by the production of ill health and electrocardiographic changes by large amounts of digitalis, these symptoms and signs being attributed to coronary disease I myself have taken, experimentally moderate to large doses of digitalis, and have not only altered my electrocardiogram with lengthening of *P R* intervals and depression of *S-T* segments and *T* waves and induced anorexia and nausea, but also caused disagreeably forceful heart action at an ordinary rate as well as extrasystoles and paroxysms of tachycardia. Atropine while producing tachycardia lowers the *T* waves of the electrocardiogram as well as does the inhalation of tobacco smoke epinephrine (adrenaline) lowers and may even invert the *T* waves in Lead 2.

In later chapters I shall take up in some detail the actual measurements, anatomic and physiologic, that are considered to be within the range of the *normal heart, blood vessels, and circulation, and shall also in later chapters* discuss symptoms and signs that may be the result of either cardiovascular diseases or of other factors not related to such diseases. There still tends to be overdiagnosis of heart disease by the erroneous application of both subjective and objective data. I have spent almost as much time in correcting wrong diagnoses of heart disease based on normal variations as I have in establishing or confirming the presence of actual heart disease One of the most common of all errors is that of including a large triangle of fat at the cardiac apex as a part of the heart shadow in roentgenologic cardiac mensuration (Figure 7)

In concluding this chapter I have still another observation to make, closely related to the present subject, and fundamental. It may well be the most important thing I shall have presented in this book. It is doubtless often a subject of thought, but there has been surprisingly little reference to it, especially as it relates to the heart. Can we tell when an organ is strictly normal? After all, what is normal? The word comes from the Latin "norma," which means rule, pattern, or carpenter s square. Normal health is supposed to be a state of the body in which disease is not discoverable. May there not be a few grams of increase in heart weight from one strain or another without lack of ease or objective evidence resulting? May there not be quite extensive change in the coronary arteries of many of us, even with narrowing and perhaps small or gradual symptomless occlusions here and there with no lack of ease and with perfectly normal electrocardiograms? And we may have to be run over at ninety or die of pneumonia which proves resistant to chemotherapy Are these coronary changes, even if they do produce electrocardiographic abnormalities *in old age, to be regarded as disease, or may they not be considered like gray* hairs as a part of the natural process of growing old? When does natural aging stop and disease begin? I find incidentally a great help in using this conception in talking to patients who are going through an acute or chronic

process of adjustment of their coronary circulation with coronary insufficiency so often a temporary state lasting but a few weeks or months or a year or two It is a comfort for the patient to realize that there is not actually a 100 per cent difference between his coronary arteries and those of his friend who feels perfectly well there may be only 3 or 4 per cent. He, himself may be just over the threshold of clinical evidence and his friend just under

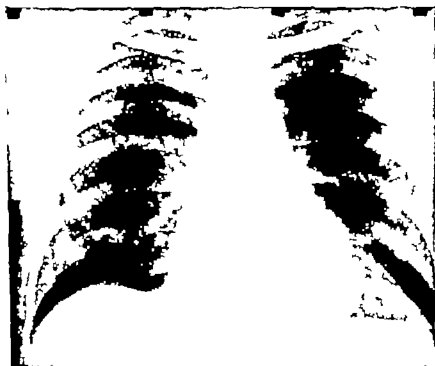


FIG. 7 Roentgenogram of healthy fat man showing large triangle f epicardial fat at the pericardiodiaphragmatic angle on the left, a common source f error in estimation of heart size.

In summary then, let me repeat that we need much more study of normal controls, than we possess at present, of the heart in all types of mankind and by all methods of examination, especially x ray analysis and electrocardiography In the past, we have all rushed to what has seemed more interesting and exciting, namely the evidence of diseased states, so that actually at the present time we are likely to be more thrilled by separating from the category of manifestations of disease certain normal findings than we are to discover disease itself. We have put the cart before the horse, but it is not too late to change about. In the study of pulse rate and blood pressure range, we do now have normal standards based on hundreds of thousands of individuals, but there is still some uncertainty as to interpretation of borderline readings especially of those in the upper range how high, for example, may blood pres

sure readings, both systolic and diastolic, rise in a normal person from nervousness alone? We need many thousands of normals for x ray heart measurements and electrocardiograms, and at the same time better correlations with body build so that we may construct more accurate tables, always avoiding, however blind worship of formulas and figures. Even statistical analysis helps us but little here for there is still a chance that an individual with measurements at the outer range of normal among thousands of carefully studied cases may himself or herself be either healthy or diseased.

Hence until we acquire adequate information and even when we have it, we can save ourselves a lot of worry and uncertainty as to whether any given individual has acquired an abnormality of the heart by following Floyer's advice and making a careful routine examination, including x-ray film and electrocardiogram, while the subject is still in excellent health. A comparison of serial data on a given person is more valuable than checking him or her against any standard tables.

Finally when all is said and done, the borderline between the perfectly normal and the slightly but definitely abnormal is so wide, not only clinically but anatomically as well, that it is unlikely that we can ever draw a sharp line between them, nor should we try too hard so to do.

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CHAPTER 3

THE PATIENT'S HISTORY AND SYMPTOMS

The present chapter and the next, after careful scrutiny as in the case of Chapter 2, have required but minor changes. They may I hope, continue to be helpful, especially to those not already expert in the field of cardiology and to those more experienced who have become careless or hurried in their history taking and physical examinations and who are still too numerous.

THE PATIENT'S HISTORY

The diagnosis and treatment of heart disease are dependent upon the history and examination of the patient. The capacity to elicit the significant symptoms and signs, the ability to analyze these symptoms and signs after they have been found, the knowledge of the best therapy and, not the least important of all, the quick appraisal of the sort of person to be treated are all essential to the satisfactory practice of medicine. In one's early days in medicine, in school and for a while afterward, the analysis of symptoms and signs and, to a lesser extent, their treatment may be learned with a fair degree of success the ability to elicit the symptoms and signs and the understanding of the individual patient and his reactions are taught less easily by word of mouth or book but come gradually with experience. Without this experience in practice one may continue but half-trained, although able to discourse learnedly on diagnosis and treatment. No amount of reading or discussion can take the place of prolonged hard work in the clinic or in the homes of patients the science of medical practice cannot be taught in the classroom.

It is therefore impossible for me to do more, in this discussion of examination and of symptoms and signs, than to point the way and to trust that eventually proficiency may come to each individual who rounds out with his own experience such information as he may find in this and other books. Any physician may and doubtless will, discover in time innovations or modifications of our present methods of examination and analysis, whereby the study and treatment of cardiovascular disease can be furthered. Progress in the last generation has been rapid and has been advanced at a fast pace in the last twenty years since the publication of the first edition of this book. We have at hand a far better chance to diagnose and to treat heart disease successfully

than had our fathers, and there is no reason why this march should not continue. With our wealth of methods of examination however there is danger that we may become overconfident or neglectful. Sometimes physicians tend to abandon old and tried methods for the new while at other times they shun new and useful methods because they fear they are but transient, or because they cannot or do not want to take the time to master them or even to understand them But often diagnosis is so difficult and signs are so misleading that we must make use of all the best tried methods at our disposal before we have properly dealt with a difficult case.

In the first part of the book which takes up the examination of patients, I shall discuss briefly the methods that have proved valuable and shall have little to say about other methods of less or of doubtful value. I shall also discuss the results of these examinations that is, the analysis of symptoms and signs, reserving for later parts of the book a detailed consideration of the causes, significance, and treatment of the cardiovascular conditions revealed by these symptoms and signs.

First and most important of all is the story of the patient himself together with a careful consideration of his personality and reactions as he tells his own story If told by someone else, especially in the absence of the patient, the story has a certain amount of value dependent on the narrator's intelligence and the closeness of his acquaintanceship with the patient, but this procedure prevents insight into the case that may come only by listening to the patient's own discussion of his history and symptoms. It has been my custom in private practice to allow a full half hour and sometimes longer for the new patient's history except in very simple or special cases. I am convinced that this time has been more profitably spent than that of any other part of the examination. Not only has it revealed direct information often of great value, but it has indirectly revealed knowledge of the type of person recounting his history and, most important of all, it has almost invariably secured the sympathetic cooperation of the patient. Detailed and careful history taking is by no means the general rule. It is, to be sure, sometimes difficult or impossible in general practice, but even when possible, it is frequently neglected, more, I believe, in Europe than in the United States. Its cultivation is worth serious effort and should not be left to a secretary or assistant. It is better to rely on an assistant's physical examination than on his history taking, if both cannot be accomplished by oneself I have also found it best for the trained physician to take his own notes of the history during the interview this is preferable to dictation to a secretary or assistant whose presence tends quite naturally to act as a check on free discussion.

The patient's history had best begin with a very detailed account of the present illness but under no condition should it be left at that. In some cases, to be sure, it may be necessary temporarily to postpone the rest of the history because of fatigue or serious illness or for another reason, but it is essential to remember that significant clues or guides to diagnosis, prognosis, and treatment may rest in the past history of illnesses, operations, or accidents in the

opinions or treatment of other doctors (often neglected, especially by hospital internes) in the social and occupational history in the account of the patient's habits, and last, but not least, especially from the viewpoint of prognosis, in the family history another frequently neglected source of information.

SYMPTOMS

The personal story of the exact onset of the very first heart symptom should be the foundation stone on which the examination of the cardiac patient rests. One sentence accurately and adequately presenting this information may be more valuable than all the other data put together An error or vagueness at the beginning may be seriously misleading. It is important to remember that not only may cardiac symptoms be confused with noncardiac symptoms but even when cardiac symptoms, pain, dyspnea, and palpitation, are actually present they may be confused with each other as in a case of paroxysmal tachycardia wrongly diagnosed angina pectoris or of angina pectoris wrongly labeled breathlessness because of hasty questioning. The development of the first symptom, its evolution, and the appearance of other symptoms must be carefully recorded according to date, circumstances, character intensity variability and relationship in order to gain full advantage from all available clues.

Symptoms are dependent on two primary factors (1) stimulation of sensory nerves, and (2) sensitiveness of the nervous system. The percentage of responsibility of each factor must be judged in every case it is constantly varying, even in the same case at different times. Thus a relatively insensitive nervous system may give rise to no symptoms even when there is apparently considerable cause for stimulation, while a sensitive nervous system may produce symptoms with very little stimulation. If fatigue lowers the threshold of the relatively insensitive nervous system, symptoms may be produced by stimulation which before was ineffective if rest raises the threshold of the sensitive nervous system, symptoms may no longer be caused by the stimulation heretofore effective.

Symptoms do not mean disease they indicate temporary disturbance of function, whether or not dependent on structural pathologic changes.

I shall consider first the three most important symptoms of cardiovascular origin—pain, respiratory disorders, and palpitation—and after that a group of less important symptoms.

Pain (ποινή, penalty) **of cardiovascular origin.** In the first place, it must be realized that pain in the chest may or may not be caused by trouble with heart or great vessels, and that heart trouble may be responsible directly for pain that is outside the chest (referred pain) even when there may be no simultaneous chest pain. There are still obscurities about the transmission and interpretation of sensory nerve impulses from the heart but an increasing interest in the autonomic nervous system in the last two decades gives promise of clearing away many of the problems (White, J C., 1935) It has, for example,

been demonstrated in recent years that cardiac pain is carried to the central nervous system by the first four or five dorsal rami communicantes on each side by way of the corresponding ganglia from the first (stellate) down, and not by way of the cervical sympathetic chains and stellate ganglia alone.

Before proceeding to the kinds of heart and great vessel pain, it is important to emphasize that discomfort due to breathlessness or palpitation is not to be called pain, although it is true that actual pain may accompany breathlessness or be induced by heart action responsible also for palpitation.

Thoracic pain for which heart and great vessels are responsible is best discussed under seven headings (1) precordial aching or heartache, and short sharp stabs of pain, (2) substernal oppression, either transient (lasting a few minutes) as in the case of paroxysmal angina pectoris or of longer duration (lasting often for hours) as in the case of acute coronary occlusion, (3) angina hypercyanotica, (4) the pain of acute pericarditis, (5) the pain of acute rheumatic carditis, (6) pressure pain from aortic aneurysms, and (7) the tearing pain of dissecting aneurysms of the aorta. Whether pain results from the acute cor pulmonale per se is as yet problematic because of the presence of the underlying acute pulmonary embolism which may itself produce great distress in the anterior thorax, or induce "coronary pain in a patient who already has considerable coronary artery narrowing, or cause pain from the resulting pleuropulmonary infarction. An interesting and important cardiac cause of *right upper quadrant abdominal pain* is acute engorgement of the liver with stretching of its capsule secondary to abrupt failure of the right ventricle It may occur paroxysmally on effort (Boyer and White, 1942) The most common or important noncardiac causes of substernal or anterior chest pain to be differentiated from the types described above are spasm of esophagus or stomach (cardiospasm) sometimes with hiatus hernia, pleurisy muscle and joint discomfort, neuritis, herpes zoster mediastinal or other intrathoracic tumors, pneumothorax and mediastinal emphysema, and neurosis.

1 *Precordial aching* or *heartache* maximal as a rule in the center of the left breast, is the commonest kind of "heart pain. It may be very mild, moderate, or very severe, and wax and wane for hours to years rarely does it last as short a time as a few minutes on any one occasion. When severe it may radiate all over the anterior thorax and even into the arms, especially down the left arm in such cases it is easily mistaken for angina pectoris. Also when it is severe it is often accompanied by precordial tenderness, which is a vitally important clue to the proper interpretation of the heartache itself The essential cause of this kind of pain is oversensitiveness of the nervous system from fatigue or other factor it is characteristic of the majority of cases of neurocirculatory asthenia (see Chapter 22) If it is found in the presence of heart disease itself it is to be interpreted only as a complication and not as a direct result of the heart disease It is, however true that the larger the heart and the more forceful its action, the more likely are heartache and precordial tenderness to be present. The pathogenesis is probably that of the thumping of the heart, whether normal or diseased, against an oversensitive thoracic wall.

Short sharp stabs of pain in the precordium are to be fundamentally explained in the same way as is precordial aching the immediate cause of such a stab as if from a pin, a needle, or a knife is in many cases a premature beat or extrasystole.

Thus, heartache and precordial stabbing sensations are unimportant and in fact often reassuring so far as serious disease is concerned, the majority of patients showing such symptoms have no heart disease at all. The idea once expressed that myocardial fatigue in chronic heart disease may produce these symptoms has not been borne out in the studies of the last decade or more. An interesting observation concerning the *side ache* that not infrequently occurs in either left or right upper quadrant of the abdomen on exertion in normal persons has been presented by Capps (1941) he ascribes this ache to anoxia of the diaphragm on either side.

2. *Substernal oppression dependent on coronary insufficiency* is also common, but it is of far greater significance than heartache so far as prognosis is concerned. It may be mild, moderate, or severe, and may or may not show transmission of pain to arms, neck, jaws, or back. Many times heartache of no importance is more severe than angina pectoris of great importance. The substernal oppression is almost invariably the result at first of considerable effort under special circumstances, such as hurrying for a train on a cold morning in fall or winter directly after breakfast, in comparison to the heart ache of neurocirculatory asthenia which occurs at any time, especially when fatigue sets in at the end of the day Substernal oppression dependent on coronary insufficiency is usually at first paroxysmal, lasting but a few minutes at a time as such it has been called angina pectoris (see Chapter 21) When it lasts for hours it is due most commonly to myocardial infarction resulting from acute occlusion of one of the main coronary arteries or branches, in almost all cases the result of thrombosis on an atherosclerotic background, but in rare cases due to embolism (see Chapter 21) Tenderness over the sternum in cases of substernal oppression does not occur unless there is a complication of neurocirculatory asthenia. Actual coronary disease, atherosclerotic or otherwise, is fundamentally responsible for the large majority of all cases showing substernal oppression dependent on coronary insufficiency in a few cases other factors, such as syphilitic aortitis, anemia, or possibly even coronary spasm itself, are wholly or in major part responsible.

Sometimes the site of angina pectoris is a little to the left of the sternum (rarely to the right of the sternum) rather than directly substernal, very infrequently is it in the middle of the left breast where the more prolonged heartache described above is located and rarely does coronary insufficiency give rise only to referred pain in one or both arms, hands, or jaws without substernal oppression—in such cases the greatest care and judgment are necessary in its interpretation.

3 *Angina hypercyanotica* is rare. A heavy pain, precordial and substernal, with or without radiation, is felt by some individuals who have considerable cyanosis, especially by a few with marked mitral stenosis or massive pulmonary

embolism, and is due probably to myocardial anoxia It has been called "angina hypercyanotica."

4 *Heart pain of acute pericarditis* is not common The majority of cases of pericarditis, acute or chronic, have no pain but if there is involvement of certain parts of the parietal pericardium, in particular that adjoining the pleura or outer diaphragmatic portion of the pericardial sac, there may be disagreeable pain resembling that of pleurisy and usually aggravated by respiration (Capps, 1927) the fact that the pain of pericarditis is almost always much increased by the act of inspiration is a very important clue in distinguishing it from the pain of myocardial infarction with which otherwise it may easily be confused. The pain originating in the diaphragmatic pericardium tends to be referred to the left shoulder An acute pericardial effusion may cause a vague dull precordial oppression.

5 *Heart pain of acute rheumatic carditis* consists of precordial pain sharper than that of the heartache of neurocirculatory asthenia but not so sharp generally as the pain of acute pericarditis although it may complicate the latter It recurs as a rule for a few days during a severe rheumatic infection in childhood. It is not a constant finding. Its pathogenesis is not clear

6 *Aortic aneurysm pressure pain* is a severe, more or less constant ache in upper thorax, neck, or shoulder dependent on pressure of the growing aneurysmal sac against surrounding tissues, especially bones, cartilage, and nerves It usually requires morphine or alcohol injection of nerves (see Chapter 28)

7 *The pain of a dissecting aortic aneurysm* is usually excruciating and tearing, located substernally or in the back, and radiating through the chest from back to front or vice versa and often down the back to the legs. It tends to be at its height at the very outset in contrast to the pain of coronary occlusion which takes a few minutes to work up to its severest intensity *It lasts for* hours and usually ends in death due to secondary rupture of the aorta into pleura, pericardium, or elsewhere. It is due to the extensive tearing of the media of the aortic wall, often through its entire length from aortic valve to bifurcation at the common iliac arteries, and in large part circumferentially also. It is likely to be confused with the pain of acute coronary occlusion (see Chapter 28)

Disorders of respiration. There are only three fundamental disorders of respiration that are related to heart disease itself. These are (1) dyspnea, that is, difficult breathing, (2) cardiac asthma, and (3) periodic apnea and hyperpnea, or the so-called Cheyne-Stokes respiration. Rapid breathing (tachypnea without dyspnea) slow breathing (bradypnea) and sighing respiration are not directly related to heart disease, although they are sometimes so misinterpreted, particularly the last named. Sighing is an important clue, when excessive, to neurocirculatory asthenia which may or may not complicate heart disease (*Figure 8* and *Chapter 22*)

1 *Dyspnea* ([illegible] difficult, and [illegible], breathing) is, of course, not pathognomonic of heart disease It has many other causes, chiefly pulmonary dis-

eases, acute and chronic, pleurisy with and without effusion bronchial asthma diseases or obstruction of the upper respiratory tract, larynx, and trachea, mediastinal diseases, diaphragmatic hernias, and certain nervous affections. The dyspnea produced by heart disease is mainly the result of a reflex action on the respiratory center from engorgement of the pulmonary circulation. Such pulmonary vascular congestion is produced most commonly by failure of the left ventricle and less commonly by the obstruction due to mitral valve deformity (stenosis, regurgitation, or both) sometimes wrongly interpreted as

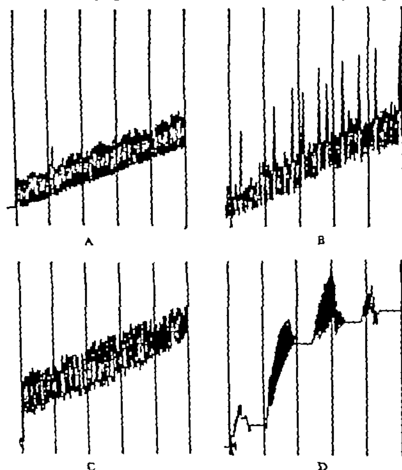


Fig. 8. Spirograms showing several types of respiration. (*A*) Normal respiration over interval of 5 minutes. Inspiration shown by upstroke and expiration by downstroke. Respiratory rate = 14 to 16 per minute. Time interval 1 minute. (*B*) Sighing respiration in case of neurocirculatory asthenia without heart disease. Ten sighs are recorded in the interval of 5 minutes. Respiratory rate = 1 to 15 (*C*) Dyspnea due to congestive heart failure. Note increase in respiratory rate from 14 to 22 toward the end of 5 minutes at which time it was necessary for the patient to change from the supine to the erect position. Note the absence of sighing respiration. (*D*) Cheyne-Stokes respiration. The durations of the three hyperpneic phases which are completely shown are 50, 55 and 50 seconds respectively and of the three apneic phases 40, 35 and 30 seconds respectively

the result of failure of the right ventricle. Actual effusion of edema fluid into the pulmonary alveoli in some cases undoubtedly adds its effect in exaggerating the dyspnea, probably chiefly through stimulating the respiratory center by the oxygen lack and increased carbon dioxide in the blood. Failure of the right ventricle with resulting stasis and disturbed gas content of the blood supply to the respiratory center is another cause of cardiac dyspnea but less common and later in appearance. Many cases with right ventricular failure, constrictive pericarditis, or tricuspid stenosis and elevated venous pressure have little or no dyspnea. It is probable that such chronic cases accommodate themselves more or less to the high venous pressure, increased blood carbon dioxide, and decreased blood oxygen in contrast to the dyspneic reaction of acutely congested cases. Moreover it is of interest to observe occasionally the disappearance of dyspnea (due to left ventricular failure) when the right ventricle fails secondarily and no longer maintains the congestion of the lung vessels.

Orthopnea (ὀρθός, erect, and πνοή, breathing) is the term applied to dyspnea sufficient in degree to force the patient to assume a sitting position, such a position acts by gravity to relieve some of the congestion in lungs and brain.

2. *Cardiac asthma* (ἆσθμα, gasping). When congestion of the pulmonary circulation occurs suddenly as the result either of acute failure of the left ventricle (*see Chapter 30*) or of tachycardia in cases of marked mitral stenosis (see Chapter 26) the tension or emphysema (ἐν, into and φύσημα, a blowing sound) that ensues may by nervous reflex action precipitate asthmatic breathing: this is cardiac asthma. It is not adequately described by any other term such as paroxysmal dyspnea or acute pulmonary edema. Of course there is always dyspnea in such cases but asthmatic respiration is a particular type of dyspnea; moreover there may or may not be clinically so-called *frank* pulmonary edema in these cases, that is, the blood vessels may be greatly engorged with or without interstitial edema but with no actual fluid in the alveoli and bronchioles. In fact the squeaking râles of pulmonary emphysema and asthma are much more common in these patients than are moist râles.

An attack of cardiac asthma most commonly comes suddenly at night when a patient with chronic heart disease is sound asleep with head and thorax low in position. It may infrequently occur on unusual effort when awake. The kind of heart disease is that causing severe strain on the left ventricle, especially hypertension, aortic stenosis or regurgitation, or coronary thrombosis, except in rare cases of marked mitral stenosis when tachycardia due to exercise or excitement or occurring paroxysmally suddenly floods the pulmonary circulation.

It is important to note that pulmonary congestion or edema may occur acutely or chronically without asthma, that asthmatic breathing occurs often without any heart disease at all, but that in an "asthmatic type" of individual "cardiac asthma" is precipitated by acute congestion of the pulmonary circulation. It is, as Hope pointed out over one hundred years ago (1832), merely bronchial asthma due to bronchiolar spasm added to and set off by heart

failure (see Chapter 30) Cardiac asthma like bronchial asthma is helped, though less dramatically by theophylline ethylene diamine (aminophyllin) administered intravenously

3 *Periodic apnea and hyperpnea* (*Cheyne Stokes respiration*) is not pathognomonic of heart disease but it occurs most frequently in chronic cardiac cases with left ventricular weakness combined with an especially poor blood supply to the respiratory center It comes on at first commonly during sleeping hours, and tends to begin in very slight degree, that is, with waxing and waning of respiration but not actually apnea and hyperpnea, it is not then such an important sign, but its progress should be watched, for when it is present during the waking hours it is a serious prognostic sign. It is the result of alternating overstimulation of the respiratory center by blood oxygen lack and carbon dioxide excess and overdepression by blood oxygen excess and carbon dioxide decrease. It is best treated by stimulation of the respiratory center by theophylline ethylene diamine (aminophyllin) or caffeine along with routine treatment of the myocardial weakness (see Chapter 30)

Palpitation (from the Latin, *palpitare* to throb) Palpitation is a much less important heart symptom than pain and dyspnea. It consists of an unpleasant sensation of the heart's action, whether slow or fast, regular or irregular It is usually the result of unimportant disturbance of heart rhythm, namely premature beats or extrasystoles and paroxysmal tachycardia (see Chapter 32) or of forceful regular heart action, rapid or slow the result of effort, excitement, toxic effect (for example from tobacco) or infection in a nervously sensitive person. Infrequently it may be caused by a more important disorder of heart rhythm such as atrial fibrillation, atrial flutter or heart block (see Chapters 33 and 34) In addition to the sensation of palpitation in the thorax there is frequently a sensation of pulse throbbing in the head or extremities, more often in the arms than in the legs. This is usually regular and forceful and due to effort, excitement, nervousness, fever thyrotoxicosis, or reaction to various substances ingested or inhaled, for example, alcoholic drinks, tobacco nitrites. It is not per se a sign of heart disease, though it is increased in the presence of aortic regurgitation or other cause of a full pulse pressure. If present in an observer it may sometimes be difficult to distinguish between his own pulse and the pulse of the subject being examined, except by rate

Other symptoms. There are several other symptoms frequently occasionally or rarely associated with heart disease but not often directly related. Exhaustion, nervousness, insomnia, dizziness, headache, cough, hoarseness, hemoptysis, faintness, syncope, anorexia, and pain in abdomen or legs are usually but incidental to various complications of heart disease examples are periodic pain in the legs on walking due to arteriosclerosis and faulty blood supply to the muscles (intermittent claudication) and nervousness due to neurocirculatory asthenia. Dizziness, faintness, and even circulatory collapse are sometimes wrongly accredited to heart disease (for example, acute coronary occlusion) when actually a severe grade of Ménière's syndrome is present, with

faulty function of the internal ear the clue rests in the presence of marked *vertigo* (with nausea as a rule) which is not a symptom of heart disease, although mild grades of Ménière's syndrome are frequent accompaniments of hypertension and the "degenerative" types of heart disease in older persons.

Several noncardiac symptoms are at times directly related to heart disease. Insomnia may be the result of a poorly defined orthopnea secondary to left ventricular failure and pulmonary vascular congestion. Anorexia and upper abdominal pain may be due to engorgement of liver stomach, and intestines, secondary to right ventricular failure. Syncope (with or without convulsions) may be the result of prolonged cerebral anemia secondary to ventricular standstill in heart block of high degree or to extreme tachycardia in paroxysms, and rarely a manifestation of angina pectoris, a sensitive carotid sinus reflex, or a vasovagal reflex of other cause. Cough, dry in character and sometimes metallic or brassy in quality may result from pressure on air passages or recurrent laryngeal nerve through the presence of aortic aneurysms, very large hearts, or massive pericardial effusions irritation of pleura or of diaphragm in acute pericarditis may also occasion cough. Both cough and hemoptysis may be due to pulmonary vascular congestion in cases of left ventricular failure and of mitral stenosis. Hoarseness may appear in rare cases of aortic aneurysms and mitral stenosis. Dysphagia may be caused by a saccular or dissecting aortic aneurysm anomalous aortic arch, dilated left atrium, or a large pericardial effusion.

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CHAPTER 4

PHYSICAL EXAMINATION

SIGNS WITH ESPECIAL REFERENCE TO CYANOSIS JAUNDICE, AND EDEMA

Having obtained the fullest possible information from the patient's own history the physician turns next to the physical examination which fills most of the gaps left in the completion of the picture of the condition of the heart. In the writer's experience the relative values of the different parts of the examination are about as follows, in percentage of the total history 45 per cent, physical examination 25 per cent, electrocardiography 15 per cent, roentgenology 10 per cent, other methods of examination (blood, urine, basal metabolic rate, cardiac catheterization, circulation rate, vital capacity and functional tests) 5 per cent.

There was somewhat of a danger of overemphasis of symptoms and of tests of reserve in the years that followed World War I to the neglect of physical signs. This situation was the result of two factors in the first place, for ten years or more before that war the pendulum had been set swinging from the extreme point of view of the nineteenth century that structural defects and evidence thereof should be the focus of medical diagnosis, prognosis, and treatment to the opposite extreme of prime consideration of the functional state of the circulation, and, secondly the need of manpower for the armed forces during *that war forced disregard for ultimate in favor of immediate prognosis*. The situation was more favorable in this respect so far as the U.S.A was concerned in World War II

Clues to the etiology of heart disease and to the functional state of the circulation are frequently found in signs other than those presented by the heart directly It is therefore essential in the physical examination of an individual suspected of having trouble with the heart to search the whole body for such clues. Hence, before taking up the examination of the heart itself I shall present the more important signs of heart trouble elsewhere in the body and discuss in somewhat more detail three special conditions—cyanosis, jaundice and edema.

In the first place the general appearance of the patient is of vital importance

this includes age, build, height and weight (and especially their relationship) nutrition, strength, mental state, color and breathing. These various points are often taken in at a glance without careful analysis but they weigh heavily in the final assessment of the case, thus affording the physician who personally examines the patient a great advantage over the doctor who is asked to make his diagnosis and prescribe treatment on the basis of hearsay evidence only no matter how careful and detailed may be the history and report of physical signs.

Head and neck. The eyes afford more clues in a cardiac patient than any other part of the body except the neck and the heart itself. Exophthalmos and related eye signs suggest at once the probability that at least some of the heart trouble is due to thyrotoxicosis. The failure of the pupils to react to light (Argyll-Robertson pupil) and their irregularity and inequality indicate at once the *need to search for aortitis itself since central nervous system syphilis* and cardiovascular syphilis are frequently associated. The arcus senilis is not an important clue, however: it is only a little more common in older individuals with heart disease than in those without. The same statement is true of cataracts. The eye grounds, on the other hand, are of considerable importance, especially when there is uncertainty about the degree, the duration, or even the past existence of high blood pressure. Important hypertension is attended in the course of a few years by sclerosis of the small arteries of the eye grounds, which becomes marked in degree and may be attended by edema, exudate, hemorrhages, and even choking of the disks, when the hypertension becomes malignant (Figure 9). Petechial hemorrhages in the conjunctivae are frequently found in subacute bacterial endocarditis.

The mouth and throat should be examined for infection of teeth, gums, and tonsils, which may sometimes lead to acute rheumatic heart disease or to acute or subacute bacterial endocarditis in persons susceptible to these diseases (see Chapters 14 and 15).

The neck may show several important abnormalities. Thyroid gland enlargement suggests thyrotoxicosis. Vigorous arterial pulsation with the subject at rest is indicative of chronic hypertension, aortic regurgitation, or aneurysmal dilatation. A tracheal tug (sometimes called Oliver's sign, Oliver 1878) is uncommon, when it is clearly evident, it points to the presence of an aortic aneurysm. Increased activity of the carotid sinus reflex, determined by firm pressure exerted by the fingers high up on the carotid artery in the region of the bulb may reveal itself in marked slowing of the heart rate, drop in blood pressure, or reflex cerebral vasoconstriction, with resulting faintness or syncope: such a finding may be helpful in explaining symptoms of obscure origin (Weiss and Baker 1933). Finally and most important of all, there is engorgement or pulsation of the jugular veins with the subject in the upright position, this means most commonly congestive heart failure involving the right ventricle or the whole heart; less often it means acute or chronic constrictive pericarditis which blocks the entrance of blood into the heart; and least often it indicates "organic" tricuspid stenosis or regurgitation or obstruc-

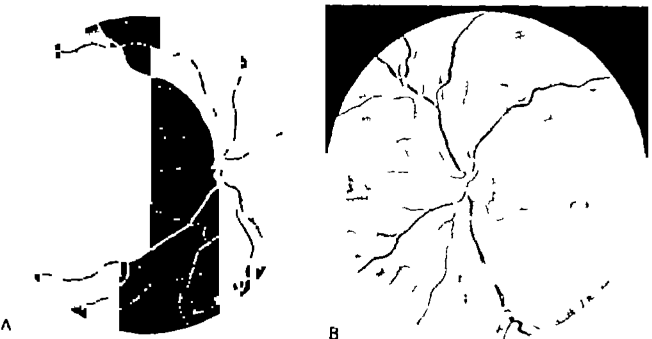


FIG. 9 Photographs of the fundus oculi. (*A*) Right eye of a normal blond man, age 23 (*B*) Left eye of 36-year old blond man with malignant hypertension, *retinal* arteriosclerosis, and generalized arteriosclerosis. Blood pressure 40 mm mercury systolic and 142 mm diastolic. Albuminuria and granular casts Retinal rteries tortuous, irregular in caliber and in various stages of sclerosis. Veins are engorged, *irregularly dilated*, and markedly compressed by superimposed teries. The superior temporal vein is bordered by white lines. Light streaks are increased on the arteries, and on the anter lor arches of the veins. The relatively normal fovea with its reflex resembles the so-called "hole in the macula owing to surrounding retinal edema. Scattered over the fundus there re two kinds of exudates one pale, yellowish-white, solid-look ing, the other (around macula) small, superficial, whit like powdered snow Radiating from the disk, in the manner of opaque nerve fibers, there are areas of retinal edema stretching into the periphery and in spots obscuring the blood vessels. There are many small retinal hemorrhages in various stages of absorption. There was similar cond ion i the right eye (Kindness of Mrs. William H. Wilmer Baltimore.)

tion of the superior vena cava by tumor aneurysm, or other mediastinal in volvement. The deep systolic jugular pulse should not be confused with the carotid pulse (see Chapter 8)

Thorax. Chest deformities have two interesting relationships to heart disease. Precordial bulging of the bony thorax without other important deformities signifies usually the development of cardiac enlargement, due to con genital defects or rheumatic involvement, during the period of early growth It is therefore valuable as a sign of important affection of the heart in early childhood. Marked scoliosis and kyphosis may themselves give rise to heart disease or more often to insufficiency of the lungs, and in rare cases a de pressed sternum may embarrass the heart (see Chapter 23) Abnormal pulsa tions and elevations of the chest wall are found in cases of aortic aneurysm (Figure 10) and of cardiac hypertrophy Palpation of the intercostal spaces



FIG. 10 Photograph showing localized bulging at the right of the upper sternum due to an aneurysm of the ascending aorta and innominate artery

in the dorsal and axillary parts of the thorax may reveal arterial pulsation *that indicate the presence of congenital coarctation of the aorta.* Cardiac pulsations will be discussed in the next chapter

Examination of the lungs is of great importance in heart disease. There may be moist râles at the bases due to pulmonary edema resulting from failure o the left ventricle, but such râles must be carefully distinguished from atelectatic râles, and from râles due to pulmonary infection or multiple infarction, distinctions which are frequently neglected. Moreover too much has been made of this sign in contrast to that of simple dyspnea or of emphysema with wheezy respiration due to the more common engorgement of the pulmonary circulation in failure of the left ventricle and in mitral stenosis of high degree. The emphysema in such cases is primarily a functional state and not usually discoverable at postmortem examination when the lung vessels are emptied; it *is due to the stiffening of the lung, fixation of the alveoli* and low position of the diaphragm with the result that relatively little air passes in and out and that only with considerable difficulty Areas of pulmonary consolidation are quite common in heart disease, especially infarcts complicating congestive heart failure or mitral stenosis. These infarcts are due to embolism from venous thrombosis in abdomen, pelvis, or legs (most commonly saphenous and femoral venous thrombosis) resulting from the slowed circulation with or without actual phlebitis, and are often serious, occasionally terminal, and frequently overlooked or wrongly labeled pneumonia much less commonly such embolism originates from the right heart chambers. Other consolidation of lung tissue may complicate heart disease, especially hemorrhagic involvement in severe active rheumatic infection, and occasionally a real pneumonic process. Finally signs of hydrothorax in a cardiac patient are common, the result of an active rheumatic pleuritis, or a part of a polyserositis which is usually of unknown etiology or most frequently a transudate due to congestive failure of the right ventricle or whole heart, involving especially the right side of the thorax. Right hydrothorax is more frequent than left either because of the greater ease of obstruction of the azygos vein on that side, or else because of higher venous pressure in the pulmonary circulation of the right lung than in that of the left lung in congestive heart failure (Dock, 1935 White, August, and Michie, 1947) Ewart's sign (Ewart, 1896 Levine and Gevalt, and Gordon, 1940) consisting of dullness, increased fremitus, and bronchial breathing at the left lung base in cases of pericardial effusion, is probably the result of several factors including compression of the lung by fluid in the pleural as well as in the pericardial cavity and pulmonary infarction.

Interstitial emphysema of the mediastinum (with or without pneumothorax) is revealed by curious crackling sounds heard over the sternum, and sometimes by palpable subcutaneous emphysema in neck or over the anterior thoracic wall (Hamman, 1939 Griffin, 1942)

Abdomen. There are three signs obtained by examination of the abdomen that are of significance in a cardiac patient. The first is enlargement of the liver from engorgement due to congestive failure of the right ventricle, to tri-

cuspid stenosis, or to acute or chronic constrictive pericarditis. If the congestion occurs quickly the liver is tender because of the rapid stretching of its capsule. Pulsation of the liver that is easily discernible is rare: it is the result either of advanced congestive failure of the right ventricle with functional tricuspid regurgitation, as in mitral stenosis of long standing, or of tricuspid valve disease (rheumatic) of high degree. Cirrhosis of the liver may be a coincidental complication of heart disease and failure, but in lesser degree it may be a sequel of chronic constrictive pericarditis or mitral stenosis of long standing. The second important abdominal sign in heart disease is splenomegaly which is confirmatory of the diagnosis of subacute bacterial endocarditis. The third sign is ascites (ἀσκός, bag or bladder) which in a cardiac patient is usually the result of congestive failure of the right ventricle but which may also be caused by tricuspid stenosis or chronic constrictive pericarditis, in both of which conditions it more or less parallels the degree of liver engorgement; ascites may also be a part of a polyserositis (Concato's disease) which forms the background for chronic constrictive pericarditis (Pick's disease) and it may likewise be caused or aggravated by a complicating cirrhosis of the liver. When the possibility of syphilitic aortitis exists inspection of the genitalia for the scar of a chancre may prove helpful.

Extremities. Abnormal pulses, dependent edema, cyanosis, clubbing of the fingers and toes, polyarticular rheumatism, and rheumatic nodules are the special signs to be looked for here in a cardiac patient. The pulse will be discussed in Chapter 8. Clubbing of fingers and toes associated with cyanosis is found in certain congenital cardiovascular defects (the morbus caeruleus) (see Figure 63, page 298). Clubbing without cyanosis is found in subacute bacterial endocarditis. However, it must be remembered that clubbed fingers are often found with noncardiac conditions, most commonly of all in pulmonary diseases; even ulcerative colitis may be the underlying cause, and a familial type of unknown etiology has been described. Recently it has been found that in all varieties of simple clubbing, except hereditary, the blood flows per unit surface or volume of finger tip are abnormally high as the result of reduction of the brachial-digital blood pressure gradients; this increase of blood flow is probably the important factor in the development of the clubbing (Mendlowitz, 1941).

Rheumatic nodules are important evidence of an active rheumatic infection but must be differentiated from the nodes of rheumatoid arthritis (see Figure 84, page 367). It is well also to palpate the dorsalis pedis and posterior tibial arterial pulses; if they are much diminished or absent, we have evidence, as a rule, of arteriosclerosis of high degree which may not be limited to the legs, or in rare cases, of congenital coarctation or of dissecting aneurysm of the aorta. Finally, absence of the knee jerks suggests the need of searching carefully for syphilitic aortitis, while their exaggeration points to the presence of a hypersensitive nervous system which may accentuate cardiac symptoms. As a rule, the more lively both knee jerks the less serious are the symptoms.

There are three particular signs in a cardiac patient that deserve consideration at some length they are cyanosis jaundice, and edema.

Cyanosis. Cyanosis (κυανος, dark blue color) of skin and mucous membranes is a sign much sought for but unless the cyanosis is well marked or constant it may be unimportant, since it often results from temporary local disturbances of the circulation and not from serious disease of heart, lungs, or blood vessels. This change in color is the result of the presence, in dilated superficial blood vessels of venous blood in which an abnormally high per centage of the hemoglobin has lost its oxygen (reduced hemoglobin) Two factors are of much importance in determining the degree of cyanosis first, the extent of oxygen dissociation or reduction of hemoglobin and, second, the degree of dilatation of the blood vessels (arterioles and capillaries) of the skin and mucous membranes which makes the cyanosis visible. The less the oxygen saturation of the hemoglobin and the more dilated the superficial vessels, the greater is the degree of cyanosis in any part of the body Arterial blood should normally be 95 to 100 per cent saturated with oxygen, which is equivalent to 19 to 20 volumes per cent (the normal oxygen content of atmospheric air) if it is but 80 to 85 per cent saturated so that it contains 3 or 4 volumes per cent of reduced hemoglobin cyanosis results. The capillary blood should normally contain about 3 5 volumes per cent of reduced hemoglobin, if it contains over 6.5 volumes per cent there results a cyanotic color like that of venous blood which normally contains about 6 volumes per cent of reduced hemoglobin. *As a rule cyanosis is most common and best seen in lips*, cheeks, ears, and hands, where the blood vessels are numerous and most exposed to the air This condition is sometimes called *acrocyanosis* (ἄκρος, outermost, and κυανος cyanosis) A further factor in the production of cyanosis is the amount of hemoglobin in the blood with an increased amount, as in polycythemia the blood possesses a much more pronounced blueness of color due to the high total content of reduced hemoglobin, than when there is dilution, as in anemia, even though the percentage of reduction of the hemoglobin is the same.

The underlying causes of cyanosis are seven.

1 The first and most common factor is local, and consists of the slowing of the peripheral circulation by cold or vasomotor nervous stimulation. Arteriolar vasoconstriction reduces the capillary blood pressure and speed of flow This slowed circulation of the blood allows a greater dissociation of oxygen than usual hence the cyanosis. If the cold becomes intense however the dissociation of oxygen stops, and even though the circulation remains very slow the skin color is red, and not blue, due to the presence of arterial blood. An abnormally high degree of sensitiveness to cold, especially in the hands, with the paroxysmal production of cyanosis (or pallor) is seen in the condition called Raynaud's disease (see Chapter 31) The high degree of circulatory disturbance in this condition is usually attended by pain Probably both cold and vasomotor nervous stimulation act together in Raynaud's disease.

2. Obstruction to the return of blood to the heart may also cause cyanosis, either from internal cause namely congestive failure of the right ventricle, tricuspid stenosis, or acute or chronic constrictive pericarditis, or from local causes, namely pressure on the veins by tumor or constriction, venous thrombosis, or incompetent venous valves. The slowing of the blood flow through the vessels of the skin causes increased dissociation of oxygen and a blue color exaggerated by capillary dilatation.

3. A third, very important, factor is congestion of the lungs due to heart trouble. A chronic engorgement of the lung vessels in mitral stenosis or acute or chronic engorgement from failure of the left ventricle causes a certain amount of blood to pass through the lungs in the middle of the dilated capillaries and so out of contact with the alveolar air continuing into the systemic circulation as venous or blue blood with a considerable dissociation of oxygen. If enough of the blood, one third it has been estimated, is so shunted from venous system to arterial system, cyanosis will result. Often combined with this factor of engorgement of the lung vessels is that of slowing of the return of blood to the heart from various causes. Thus one factor may reinforce another in the production of cyanosis.

4. Certain congenital heart defects may cause cyanosis by shunting venous blood directly into the systemic circulation via a single ventricle or dextroposed aorta overriding both ventricles, or in transposition of the great vessels, or less commonly and later in life, through interventricular or interatrial septal defects or patent ductus arteriosus. It has been calculated that 30 to 40 per cent of the venous blood must be so shunted in order to assure the presence of cyanosis. In patients of this type the capillaries of the skin have been found dilated and the peripheral circulation slowed, and it has been suggested that this local factor may be more important in the production of cyanosis than the congenital heart disease itself. It is likely however that the veno-arterial shunt alone is responsible for most of the cyanosis which is in turn deepened or perhaps even brought to notice by the slowing of the peripheral circulation the slowing of the peripheral circulation is occasioned by the need of the tissues to remove sufficient oxygen from the oxygen-deficient blood stream. The polycythemia present in most cases of congenital heart disease with a right to left shunt is an additional factor which exaggerates cyanosis. Congenital heart defects in which there is no veno-arterial shunt are not attended by cyanosis unless there is a complicating factor of congestive heart failure or pulmonary disease.

5. Disease of the lungs, acute or chronic, may be a cause of cyanosis, the presence and degree of which are dependent on the amount of pulmonary involvement and on the presence of complicating factors. With consolidation of much lung tissue in pneumonia, or infarction, venous blood in sufficient amount to cause cyanosis is shunted through the pulmonary circulation without coming into contact with alveolar air. Moisture in the alveoli and bronchioles may act even more than consolidation to cause cyanosis by preventing contact of blood with air as is the case with severe influenza or

inversely but not in the same degree. In nephrosis and starvation edematous fluid is very low in protein, giving percentages lower than in any other conditions, while the fluid from lymphedema and also from edema in inflammatory areas has a high content of protein, the more purulent the inflammatory edema is, the higher its protein content and the nearer it approaches the chemical state of blood serum *The specific gravity of edematous fluids varies with the* protein content, from about 1 008 with very little protein to 1 020 or more, approaching the specific gravity of blood serum itself Ascitic and hydrothoracic fluids or so-called transudates in congestive heart failure have the same composition as subcutaneous edema fluid except for a somewhat higher protein content and a higher specific gravity (about 1 012)

Most of the underlying causes of edema are known. In the first place, there is the simple effect of gravity Standing long in one position with little or no movement of the legs (contraction of the leg muscles favors an upward flow in the veins) causes a slowing of the circulation with increase in size of the legs from stasis, progressing in extreme cases to actual edema, which is usually most evident in the ankles just above the shoes and over the shins. Thus edema becomes palpable, it is said, when the limb volume has increased by 8 per cent. The heavier the person and the longer the time on the feet, the more likely is the appearance of edema. This edema may be regarded as a physiologic occurrence when it is found in heavy persons who stand much of the time. Walking or other movement of the feet and legs aids the circulation and tends to prevent edema. The presence of varicose veins favors its occurrence especially unilaterally or preponderantly in one leg or the other

Besides gravity a common cause of edema and one of the most frequent is obstruction to the return flow of fluid from tissues to heart. Lymphatic block is rarely the cause of any important edema, although it may in exceptional cases give rise to chronic massive increase in size of legs or arms or genitalia, called elephantiasis. Obstruction of the venous circulation is frequently responsible for edema. This obstruction may come in a variety of ways (1) *by venous thrombosis, due to inflammation or to stasis,* (2) by pressure on veins from without, by tumors, scars, and tight bands, and more or less normally late in pregnancy (in the last four weeks) and (3) by resistance to the flow of blood into the heart, usually because of the inability of the right ventricle, from failure or otherwise, to pass on all the blood it receives. This venous obstruction also may be due to tricuspid stenosis or to limitation of the size of right heart chambers and venae cavae by a large pericardial effusion or by chronic constrictive pericardial adhesions (as in Pick's disease) so that too small an amount of venous blood enters the heart in diastole with resulting accumulation of edema fluid in tissues and serous cavities. The explanation of edema secondary to obstruction of the return flow of blood to the heart from any cause is the increased hydrostatic pressure in the venous ends of the capillaries which results from the increased pressure in the systemic veins and which prevents the normal absorption of fluid from the tissues. Krogh, Landis, and Turner (1932) demonstrated that excessive

fluid accumulates in the tissue spaces in man when the venous pressure (normally 6 to 8 cm of water) is raised above 15 to 20 cm.

Another important type of edema, but much less common than that resulting from venous obstruction with or without cardiac cause, is that dependent on physiochemical factors which produce a disturbance of the normal osmotic pressure relationship between the fluids in capillaries and tissues. Here disorders of either liver or kidneys may play an important role, with the onset of a spontaneous diuresis heralding a beginning recovery The higher concentration of substances, in particular proteins, which diffuse with difficulty through the capillary wall, in the blood stream than in the body tissues establishes an osmotic pressure which normally draws fluid from tissues into the blood and so tends to neutralize the hydrostatic pressure so far as the fluid balance on both sides of the capillary walls is concerned. Nephritis, especially with nephrosis, and disturbances of tissue metabolism due to starvation are frequently associated with edema this edema is usually general in distribution, affecting face, arms, and hands, and not simply the dependent portions of the body as in congestive heart failure Nephritic edema is due fundamentally to damage to the renal tubules which prevents the concentration of the urine and the reabsorption of albumin the low content of albumin in the capillary blood serum prevents the proper return flow of fluid by osmotic pressure into the blood from the tissues. A certain type of nephritis with free loss or leakage of sodium tends, like Addison s disease with its faulty sodium metabolism, toward dehydration and collapse and not edema.

Edema secondary to decreased negative osmotic pressure of the blood may be added to edema due to increased positive hydrostatic capillary pressure in a patient with congestive heart failure and malnutrition this is a point of much importance and explains obscure findings in some cases. The excessive ingestion of sodium chloride, particularly in cases of low myocardial reserve, also favors the accumulation of edema in the body tissues.

Another important cause of edema in congestive heart failure seems to be due to deficient circulation to the kidneys secondary to failure of the myocardium of the left ventricle or of the whole heart and resulting in inability of the kidneys to excrete sodium normally the retention of sodium results in the building up of the body water both in and out of the circulation.

Recently Sarnoff (personal communication, 1951) has found that in experimental animals excessive stimulation of the vasomotor center in the brain can result in such peripheral vasoconstriction that blood is rapidly transferred in bulk from the systemic circulation to the pulmonary circulation, resulting in pulmonary edema this is probably an explanation for the so-called neurogenic or cerebral type of pulmonary edema.

The metabolic disorder of hypothyroidism (myxedema) is commonly associated with a nonpitting accumulation of fluid in the body tissues generally (not primarily in dependent parts of the body) and is attended by a low blood plasma volume in contrast to cardiac edema, thyroid therapy clears this myxedema.

Beriberi (avitaminosis) is attended by the accumulation of fluid in body tissues but rarely by frank edema.

A rare type of edema of unknown cause is hereditary in nature (Milroy 1892 Braham and Howells, 1948)

There are two other varieties of edema that need little comment here because of their ease of recognition and their absence of connection with cardiovascular disease (1) local tissue edema associated with an infectious or toxic process, the commonest kind of edema of all, and (2) angioneurotic edema (Quincke, 1882) also generally localized.

Edema due to heart disease may be of any degree, from slight edema of the lungs, or over ankles or shins developing after a considerable length of time in the standing position, to massive edema (called *anasarca* ἀνά, upon or throughout, and σάρξ flesh) of much of the body in extreme cases even affecting the arms, chest wall, and face. With extensive cardiac edema, fluid tends to accumulate also in the peritoneal cavity (ascites) pleural cavities (hydrothorax) especially the right where it appears earlier than in the left, and even in the pericardium (hydropericardium) Edema of one side of the body (as of face, arm, chest, abdominal wall, or leg) may sometimes be more marked than that of the other side It may be found that this is the effect of gravity the patient having been lying on that side of the body When, however in an ambulatory patient edema is confined to one leg, or is much more marked in one leg than in the other local venous obstruction (or vasodilatation) is the probable cause. Cardiac edema may be associated with some other type of edema in the same case.

Edema of the brain is the result of infection, hemorrhage, infarction, or toxic influences such as alcoholism Its occurrence in heart disease is not clearly recognized even when there is extensive anasarca involving the upper part of the body in the course of extensive congestive heart failure. Edema of lungs may be found in noncardiac patients as the result of infection, infarction, nephritis, or toxic state, or as an unusual reflex to pleural trauma or to central nervous system disease when of cardiac origin it results from failure of the left ventricle or from obstruction to the entrance of blood into the left ventricle by marked stenosis of the mitral valve. It is to be noted that pulmonary edema is due to left ventricular failure and not to right ventricular failure In fact, when right ventricular failure follows failure of the left ventricle, as often happens, congestion and edema of the lungs decrease and sometimes disappear entirely Edema of the liver and other abdominal and pelvic viscera, is commonly due to failure of the right ventricle or of the whole heart, to marked tricuspid stenosis, or to acute or chronic constrictive pericarditis. Edema of heart and skeletal muscle is not common It has been noted in extensive general anasarca and in beriberi.

Finally it is to be noted that bilateral pitting edema of the legs is much less commonly due to heart failure than to other causes, especially local venous circulatory fault, even in cardiac patients themselves. Much digitalis has been wastefully prescribed in such cases before careful appraisal of the heart itself

has demonstrated its futility in these patients, of course heart failure may by chance eventually supervene and then digitalis may clear the new increment of edema.

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CHAPTER 5

PHYSICAL EXAMINATION OF THE HEART ITSELF

INSPECTION PALPATION PERCUSSION, AND AUSCULTATION

This chapter and the next along with Chapters 3 and 4 concern themselves with the simplest and yet the most fruitful methods of examination, requiring only the use of the voice, the ears, the eyes, the fingers, the stethoscope, the blood pressure instrument, and especially the intelligence, all of which are at once available to the practicing physician. Time and effort supply the necessary experience.

One is very prone in these days of the machine age to abandon the patient training and skilled use of the unaided senses. Nowhere is this truer than in the practice of medicine. It has become rather too easy in hospitals or even in the doctor's office to make a roentgen ray examination of the heart and to neglect inspection, palpation, and percussion. But the senses of sight, touch, and hearing unaided by instruments, except for the simple convenience of a stethoscope and of a sphygmomanometer are still well worth cultivating. *When the senses are highly trained and skillfully used they establish* such a justified feeling of confidence that it is possible to obtain much information about heart size and shape even when the roentgen ray is not available, and also to secure other important data about the heart not shown by the roentgen ray as in the case of palpable thrills and changes in heart sounds and the presence of murmurs which reveal much concerning the structural changes in the heart *and its functional condition.*

INSPECTION AND PALPATION

The first important thing to attempt to do on examination of the heart is to locate *the position of the apex* best done with the subject seated and the thorax inclined slightly forward. This is possible in the great majority of cases, failing only in a few obese or very sick patients. Both inspection and palpation aid in this purpose, but more especially palpation, which, by the use of the trained fingers, permits the identification of the maximal impulse as the site of the cardiac apex. Such identification is usually in agreement within a few

millimeters with the position of the apex as determined by orthodiagraphy A measurement of the horizontal distance of the maximal apex impulse from the midsternal line tangentially to the front of the chest is recorded in centimeters and compared to the position of the "midclavicular" line which is a vertical line dropped from a point halfway between the midsternum and the outer end of the left clavicle as noted below (Figure 11) The position of the cardiac apex should lie in the left fifth intercostal space in or to the

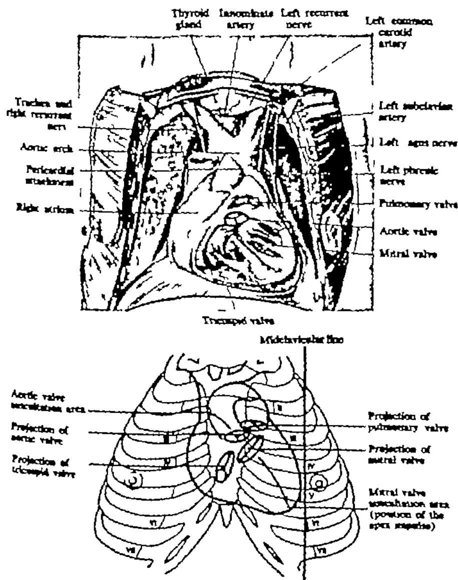


FIG. 11 Topographic relationships of the heart and great vessels The heart chambers and blood vessels are shown in distended state. (Corning, *Lehrbuch der topographischen Anatomie* 1917)

right of the midclavicular line in a normal adult sitting or standing, except in rare instances when the heart may be displaced upward and a little outward from great abdominal distention, as in pregnancy. The average position of the midclavicular line in the normal adult is 8 to 8½ cm to the left of the midsternum, varying from 7 to 10 in the extremes of body size. The maximal apex impulse falls normally on this line or ½ to 1 cm within it; rarely when the thorax is long and the heart vertical in position so that it is almost centrally placed in the chest, the cardiac apex is low, often behind the sixth rib or rarely in the sixth intercostal space and as much as 1½ to 2 cm medial to the midclavicular line. If it is beyond the midclavicular line in the fifth space, enlargement of the heart is to be diagnosed unless the heart is displaced by fluid or air in the right pleural cavity, by a depressed sternum, or by retraction of the left lung and pleura. If the heart is displaced upward appreciably its apex tends to lie in the fourth intercostal space or behind the fifth rib and may then be normally slightly (½ to 1 cm) beyond the midclavicular line. In infants and very young children, especially when they are fat, the apex impulse is normally often in the fourth intercostal space just beyond the midclavicular line.

Certain changes of body position and of the height of the diaphragm cause considerable shifting of the position of the apex impulse, when the heart is normally freely movable. The three greatest shifts are produced as follows. (1) a change from the left to the right lateral decubitus causes a shift of the mediastinum and its contents, including the heart, laterally, the cardiac apex impulse moving often as much as 4 or 5 cm from left to right, from out toward the anterior axillary line to a point not far to the left of the sternum; such a shift does not markedly affect the angle of either the anatomic or the electric axis and so produces little change in the electrocardiogram, which in part explains why such a test of change of position is of little value in the diagnosis of adhesive pericarditis. (2) A change in the height of the diaphragm produced readily by deep breathing alters appreciably the position of the apex impulse both laterally and vertically from, say, a point in the midclavicular line underlying the fifth rib to a point 1 to 1½ cm inside the midclavicular line underlying the sixth rib; such a shift does markedly affect the angle of both anatomic and electric axes of the heart and so produces usually a striking change in the electrocardiogram, particularly in Lead 3 (see Figure 4, page 33). (3) A change from the supine to the standing position alters somewhat the position of the apex impulse, partly by straightening out the heart (that is, in slight to moderate degree making it more vertical), partly by producing a rotation from left to right, and partly by causing a drop of the heart as a whole; the result is somewhat like that caused by deep inspiration but not so pronounced and more complicated in mechanism; the effect on the electrocardiogram is very variable but usually not marked (see Chapter 9).

Finally it is to be noted that the nipple line is not a suitable guide to heart size, chiefly because of its great variation in distance from the midsternum in

individuals of the same size (as much as 2 or 3 cm in extreme cases) but also because as a rule its position is normally 1 to 2 cm beyond the site of the cardiac apex.

The major pulsatory movements of the thoracic wall which may be seen and felt, resulting from the action of an enlarged heart are often complicated but their analysis may aid in elucidating the heart condition they have been made the subject of a monograph by Dressler (1933 and 1937) A few major points of interest are the rocking movement of the thorax when the left ventricle is very large and forceful, the left thoracic wall moving outward and the right inward in systole and vice versa in diastole the forward thrust of the anterior thoracic wall with retraction of both lateral walls in systole when the right ventricle is very large and strong, together with a visible and palpable forceful impulse in the region of the pulmonary artery in some such cases when the chest wall is not too thick, and an outward thrust of the right chest wall in systole when the atria are markedly enlarged, as in the case of the occasional huge left atrium found in advanced mitral valve disease and of the large right atrium in tricuspid valve disease, the outthrust being due not to atrial contraction but to the forceful ventricular pulse transmitted directly into the atrium through the incompetent valve. These are more or less major pulsatory movements in addition to the apex impulse itself. When the heart is much enlarged and its action forceful the fifth and sixth ribs are outwardly displaced at each heart beat.

Two other points about cardiac pulsation are worthy of comment. First, a very active heart, whether enlarged or not, will produce such a forceful apex impulse that it is widely felt and may be misleading· it is the maximal point of this impulse, or rather a few millimeters beyond but not its furthest point out, that marks the position of the apex itself. Second, a systolic re traction of the fourth and fifth intercostal spaces just to the left of the sternum, often well seen in a person with a thin chest wall, is a normal occurrence when the heart is not enlarged or when only the left ventricle is enlarged, and it is not to be interpreted as the result of pericardial adhesions it is due to the withdrawal of the right ventricle from the chest wall when it contracts against the left ventricle, which in turn contracts away from the region of the sternum but thrusts its apex up against the chest wall further to the left, that is, in or beyond the midclavicular line depending on the size of the left ventricle.

Thrills. The next observation to make in physical examination of the heart is to palpate the precordium for thrills, which are often difficult to feel with the untrained hand unless they are very marked in degree exercise, by increasing heart action and blood flow helps to make thrills that are faint more evident; when a thrill is suspected and is not brought out by exercise it probably does not exist. Thrills are relatively rare, accompanying a few murmurs only especially the aortic systolic murmur of aortic stenosis and the mitral diastolic murmur of mitral stenosis. Valvular regurgitation produces thrills in only the rarest cases, whether from aortic regurgitation, mitral regurgitation, or pulmonary regurgitation, and then usually when the valve has an odd deformity

such as eversion or rupture of an aortic cusp or a rupture of mitral cusp or of chordae tendineae.

A systolic thrill felt over the precordium but best in the second intercostal space just to the right of the sternum (so-called aortic valve area) and transmitted into (but not limited to) the vessels of the neck is due as a rule to aortic or subaortic stenosis, rarely to an aortic aneurysm It is of interest and importance that such a thrill may be felt well also at the cardiac apex. A systolic thrill, felt usually in a narrowly localized area, in the second intercostal space just to the left of the sternum (so-called pulmonary valve area) means in most instances congenital stenosis of the pulmonary valve or of the infundibulum of the right ventricle, rarely patency of the ductus arteriosus or extreme dilatation of the pulmonary artery A systolic thrill, also usually very limited in extent, felt in the fourth intercostal space just to the left of the sternum indicates as a rule the presence of an interventricular septal defect. A diastolic thrill, middiastolic or presystolic in time, felt in a small area at the cardiac apex and a little toward the midsternum from the apex is characteristic of a high degree of mitral stenosis but is also found in rare cases of marked dilatation of the left ventricle with rapid blood flow (see Chapter 14) A continuous thrill, rather rare, felt in the second intercostal space just to the left of the sternum is found in a few cases of patency of the ductus arteriosus, or to the right in the extremely rare instances of right aortic arch or dextrocardia plus patency of the ductus arteriosus such a thrill is also characteristic of an arteriovenous communication (called aneurysm) anywhere in the body

Finally it should be noted that the search for thrills may be misleading for three important reasons (1) they may not be felt even in the presence of loud and important murmurs, as, for example, in some cases of aortic stenosis, (2) they may be suspected when there is actually nothing wrong, and (3) they may be felt in almost unique cases where no murmur can be heard due to the inaudibility of vibrations of very low pitch which are nevertheless of importance

PERCUSSION

Before turning to the subject of cardiac auscultation later in this chapter I welcome the opportunity to say a few words about the much neglected and often despised method of cardiac percussion (*percutere* to strike) Percussion of the heart is valuable in the first place because it aids in determining heart size and shape when it is not possible to carry out a roentgen ray study a procedure that continues to be difficult or impossible in the case of quite a few patients. Secondly it is of help in occasional cases when the apex impulse is felt with difficulty or not at all. And, thirdly it serves as a check on the accuracy of reports of roentgen ray measurements. Considerable training and experience are necessary before one can properly rely on the accuracy of cardiac percussion, but such training and experience are not difficult and

they are well worthwhile. The method of percussion matters little, that is, whether direct (immediate) or indirect (mediate) whether one uses the finger or special instrument as the pleximeter and whether a hard stroke or a gentle stroke is employed (a light stroke is preferable when the chest wall is thin and the heart near to its surface, and a heavier stroke when the chest wall is thick or some emphysema of the lungs is present) The main point is to adopt a definite technic and to stick to it until one becomes expert in its use, constantly comparing at first the results obtained with the heart measurements by orthodiagram Percussion involves not only the sense of hearing but also that of touch.

Auenbrugger Leopold. *Inventum Novum Ex Percussione Thoracis H mani* Vienna, 1761

From John Forbes English translation, 1824

"I. The thorax of a healthy person sounds, when struck.

"II. The sound thus elicited from the healthy chest resembles the stifled sound of a drum covered with a thick woollen cloth or other envelope.

"III. Over the space occupied by the heart the sound loses part of its usual clearness and becomes dull

"IV The thorax ought to be struck, slowly and gently with the points of the fingers, brought close together and at the same time extended.

"Scholium. Robust and fat subjects require a stronger percussion such, indeed, as to elicit a degree of sound equal to that produced, by a slight percussion, in a lean subject.

"X. To be able justly to appreciate the value of the various sounds elicited from the chest in cases of disease, it is necessary to have learned by experience on many subjects, the modifications of sound, general or partial, produced by the habit of body natural conformation as to the scapulae, mammae, the heart, the capacity of the thorax, the degree of fleshiness, fatness, and so forth.

"XLVI. Signs of Hydropericardium. The sound in the cardiac region is now as completely deadened as if the percussion were pplied to a fleshy limb.

"XLVIII. When the heart becomes so much distended by blood, accumulated in its auricles and ventricles, as to be unequal to propel forward its contents, it frequently becomes thereby enormously dilated. This dilatation has been called Aneurism of the Heart.

"The pathognomonic sign of this affection is the complete fleshy sound on percussion existing over a considerable space in the region of the heart.

In the course of one s palpation and percussion one may elicit an important symptom, namely *precordial tenderness* which, in the absence of local trauma or lesion of the chest wall itself is useful evidence of a high degree of nervous sensitivity or fatigue, as in cases of neurocirculatory asthenia, it is found usually in the absence of heart disease (see Chapter 22)

It is well to percuss first the cardiac apex, beginning in the left axilla and working toward the sternum. One observes a pronounced change of note and resistance when one reaches the apex (usually 7 to 9 cm to the left of the

midsternum in the normal adult) and this point agrees within a centimeter with that of the maximal apex impulse It tends to be a few millimeters further to the left. It is to be compared, as is the site of the apex impulse, with the midclavicular line. Next, it is best to percuss the left border of the heart in the third and fourth intercostal spaces an increase of heart size toward the left is usually made out readily and here again there is close agreement as a rule between percussion and orthodiagraphic measurements.

Percussion dullness in the third intercostal space to the left of the sternum should not normally exceed one half the distance from midsternum to apex (that is, not more than 3 to 4½ cm according to the size of the individual) It often measures less. If it does exceed this, we have evidence of abnormality in heart size or shape or both. It may be too far to the left even when the apex impulse is in the normal position such a finding is usually indicative of mitral stenosis, an atrial septal defect, or congenital patency of the ductus arteriosus, for the measurement records the size of the left atrium near its appendage and of the trunk of the pulmonary artery

The reason why the left border of the heart can be so well percussed in most cases is because it lies close to the anterior chest wall, especially in the sitting and standing positions. Obesity and pulmonary emphysema and, rarely widely transmitted abdominal tympany may interfere with percussion of the heart.

We find a very different situation when we try to percuss the great vessels in the first and second intercostal spaces to left and right of the sternum and under the upper sternum itself. It is difficult or impossible to outline these structures when they are normal, and sometimes even when they are enlarged, because of their small size, their distance from the anterior chest wall, and their proximity to resonant air passages and lung apices. Only when there is a pronounced abnormality as in the case of an aortic aneurysm, does one find increased dullness by percussion to the right or left of the upper sternum respectively It is generally convenient to make a record that there is no abnormal dullness in the region of the great vessels, except in the infrequent cases where there is such abnormal dullness, rather than to attempt to distinguish doubtful percussion borders. The same is true of percussion of the right side of the heart in the attempt to outline the position of the border of the right atrium It is impossible to percuss accurately this heart border because of its distance from the anterior chest wall, there being an error of 1 to 1½ cm under the best of circumstances (the right border of the right atrium in the normal adult is usually about 4 cm to the right of the midsternum, while the dullness by percussion extends only 2 to 2½ cm to the right, just barely beyond the right edge of the sternum) Clearly defined dullness to percussion in the third and fourth intercostal spaces more than a centimeter to the right of the right edge of the sternum almost always means enlargement of the heart in whole or in part, or displacement of the heart to the right, or a pericardial effusion rarely this may be found normally when the chest wall is very thin. As a rule, therefore, it is convenient to say that there is no ab-

normal dullness to the right of the sternum, when such is true, rather than to give measurements which are misleading as to actual heart size.

Finally we need no longer trouble with the old designations "absolute" and "relative cardiac dullness" they serve no useful purpose.

AUSCULTATION

Laennec, R. T. H. *De l'auscultation médiate* Paris, 1819 Brief extracts translated by myself.

About three years ago I began the research, the result of which I am publishing today

"Some physicians have tried to apply their ears to the precordial region in these cases. The heart beat perceived thus simultaneously by the senses of hearing and of touch becomes more evident. This method is, however far from giving the results it would seem to promise. I have found it dvised nowhere. As uncomfortable for the physician as for the patient, the method is so disagreeable that it is practically of no use in the hospitals, it is hardly to be suggested in the case of most women and in some of them it cannot be employed at all because of the size of the breasts.

I was consulted in 1816 by a young woman who presented general symptoms of heart disease and in whose case the application of the hand and percussion gave little information because of her obesity Since the age and the sex of the patient forbade my using the method of examination already described (that is, immediate auscultation) I happened to recall a well known acoustic phenomenon If one applies the ear to one end of beam, one hears very distinctly a pin scratch at the other end. I thought that I could profit by this physical property in the case of the patient under discussion. I took a sheet of paper rolled it up tightly applied one end of this cylinder on the precordial region, and, placing my ear against the other end I was as surprised as pleased to hear the heart beat in a manner much more clear and distinct that I had ever done by pplying the ear immediately to the chest.

"I use at present a cylinder of wood pierced in its centre by a tube three lines in diameter and divided in the middle by a screw joint in order to make it more portable.

Auscultation of the heart (*auscultare* to listen) has become a time-worn method of examination and is considered by some to be old-fashioned and unworthy of especial attention, but it remains today a source of vital information about the heart and it has actually advanced in importance in the last two decades because of the better understanding of its findings. Like percussion it demands careful training and long experience for its mastery but the time spent on it is exceedingly worthwhile. Because of our present knowledge about heart sounds and murmurs, even direct or immediate auscultation may be practiced with far better success than in the days before Laennec introduced the stethoscope for indirect or mediate auscultation in 1819 but the use of the ear directly applied to the chest is clumsy and inconvenient and does not allow the detection of the fine shades of tone and intensity that is

possible by the use of a stethoscope. The most useful instrument is binaural with two easily adjustable chest pieces, one a bell and the other a flat resonating chamber with diaphragm (Bowles chest piece) which have a somewhat selective action. For physicians who are hard of hearing and for amphitheater clinics, audion tube amplifiers are now available. With earphone connection there is very little distortion of sounds and murmurs this method has proved to be well worthwhile in demonstrations to large groups during the past few years.

Auscultation of the heart should be carried out at the cardiac apex (mitral valve area) in the second intercostal space just to the right of the sternum (aortic valve area) in the second intercostal space just to the left of the sternum (pulmonary valve area) at the left of the mid and lower sternum (septal and tricuspid valve areas) and in the left axilla, lung bases, and neck for transmission of murmurs. Both bell and Bowles chest pieces should be used, and if there is any possibility of mitral stenosis and the murmur thereof is not heard with the subject in the upright position it should be sought with the subject supine or lying on the left side, and after exercise. It is also worthwhile to listen routinely over the thoracic spine in a search for the continuous murmur caused by coarctation of the aorta.

An interesting application of the principle of selective binaural timing of sounds and murmurs to ascertain their points of origin and directions of transmission, for example, from cardiac base toward apex or vice versa, has been introduced and perfected by Kerr and his associates (1937) this acoustic principle is similar to the optic recognition of distances and timing by binocular perspective vision. The instrument devised for this purpose has been called the symballophone and can be used helpfully provided the hearing is equal in both ears (they should be accurately tested) and provided experience in the use of the symballophone is gained by practice inertia has delayed any general adoption of this innovation.

Phonocardiography (also called stethography in the past) the graphic recording of heart sounds and murmurs by electric reproduction, using microphone, amplifier and galvanometer has gradually reached a good state of development during the past generation and can usefully supplement the personal use of a stethoscope by a trained observer especially in the exact timing of sounds and murmurs in problem cases. Two difficulties have yet to be eliminated, the first that of the frequent addition of artifacts from extraneous sounds or electric currents to the heart sound records, and second that of the sometimes inadequate reproduction of certain murmurs, especially the fainter diastolic murmurs of low or high pitch. However these difficulties have been largely surmounted. One additional benefit may eventually accrue through this technical method of study namely extra information about the state of the heart from variations in inaudible vibrations picked up by the apparatus but which have not as yet received adequate clinical analysis. Classroom amplification of heart sounds and murmurs by the additional use of a loud-speaker needs further perfection.

There were published some years ago (Rappaport and Sprague, 1941 and 1942) two interesting and valuable papers on the physiologic and physical laws that govern auscultation, and their clinical applications, with especial reference to phonocardiography· their conclusions are worthy of direct quotation. Their 1941 paper was summarized as follows

Rappaport, Maurice B E.E., and Sprague, Howard B., M.D. "Physiologic and Physical Laws that Govern Auscultation, and Their Clinical Application." *Am. Heart J* 1941 XXI, 257

"1 *Tones of different periods of oscillation or frequency but of similar intensity* affect the human ear to different degrees. The audiogram, which is a graphic representation of the threshold of audibility is a measurement of the degree to which human hearing varies with respect to the frequency of vibration of the stimulus.

"2. The minimum change in intensity of a sound stimulus to which the human ear is capable of responding varies with the general level of the sound, as well as with its frequency In the auscultatory frequency band, as the frequency of the stimulus is lowered, a decidedly greater percentage variation in intensity is therefore required to produce the minimum perceptible change.

"3. The human ear is a better detector of changes in frequency than of changes in intensity A sound stimulus with a high sensation level requires less of frequency variation to produce minimum susceptibility than does a sound stimulus of a lower sensation level. Also, the ear is somewhat less sensitive to frequency variations at the lower end of the auscultatory frequency band than it is to variations in the upper region.

4 In the auscultatory frequency band, the frequency of a stimulus may be varied rapidly over a considerable portion of an octave without detection by the ear

"5 The auditory sensation produced by a complex sound may be decidedly different in character as well as in intensity when the stimulating level is decreased or increased, even though no distortion is introduced. As a complex sound, such as a murmur becomes more intense, the low-pitched components appear more prominent to the observer

"6. When a sound of comparatively high intensity immediately precedes a sound f considerably lower intensity masking of the sound of lower intensity may result.

"7 There are many paths along which heart and chest sounds travel in the human body in order to reach the surface. As a result, a large percentage of the sound energy never reaches the surface because of viscosity elasticity density spreading, reflection, and refraction losses.

"8. The entire auscultatory frequency band for heart sounds and murmurs lies below 1,000 cycles per second. An estimation f the lower frequency limit of heart sounds and murmur components puts it in the vicinity of 5 to 10 cycles per second, although 30 to 40 cycles per second is the lower limit of audibility

"9 Acoustic stethoscopes may be classified as either monaural, binaural, or differential. Either the monaural or binaural stethoscope may be employed for general auscultatory purposes, whereas the differential stethoscopes are primarily instruments for localizing and comparing sounds.

10. The open stethoscopic chest piece, or bell, when applied to the patient's

chest, may be considered as a diaphragm type of chest piece. The skin which is bounded by the lip of the bell forms the diaphragm, and the fleshy portion under the skin acts as a damping medium.

"11 The larger the diameter of the open stethoscopic chest piece, the better its response to low-pitched sounds. This is accomplished at the expense of the higher frequency components.

"12. The greater the pressure with which the open stethoscopic chest piece is applied to the patient's chest, the better is the response of the stethoscope to higher frequency components. Thus, by varying the application pressure, the physician exerts a variable filtering action upon the sounds because the natural period of the skin diaphragm bounded by the chest piece depends on the application pressure.

13 Open stethoscopic chest pieces of various geometrical shapes have been devised to improve the sound-accumulating efficiency of the stethoscope. A bell with its interior shaped like a parabola has been a favorite. Such chest pieces invariably decrease the efficiency of the stethoscope because they increase the internal volume of the chest piece.

14 The only important consideration when designing an open stethoscopic chest piece is to keep its internal volume at a minimum and have it so shaped that, in the case of an obese patient or one with an inelastic chest wall, the bell will not fill with flesh to such an extent as to decrease effectively the diameter of the enclosed diaphragm.

15 The diaphragm type of chest piece (Bowles type) which is commonly used in auscultation is especially useful in detecting faint, high-pitched sounds. When it is applied to a patient's chest, the principle of operation of the Bowles chest piece is similar to that of the open bell, except that additional attenuation of the lower pitched heart and chest sound components is obtainable with the Bowles chest piece, and this prevents masking of the higher pitched components.

16. In the Bowles chest piece, as in the open type of chest piece, the air volume should be made as small as possible in order to obtain maximum efficiency

17 Between 60 and 400 cycles per second, which includes most of the auscultatory region, tests show that the binaural method of auscultation through rubber tubes is, on an average, 20 decibels better than the monaural method, with the ear directly applied to the stethoscope. A 20-decibel difference is equivalent to a tenfold increase in sound pressure at the ear drum. Only between 850 and 1 000 cycles per second is monaural, or direct, auscultation more efficient than binaural, and this range is too high to be practically useful.

18 The changes in the efficiency of an acoustic stethoscope which are caused by varying the length of the tubing, although they are not given any consideration by stethoscope users, produce an effect upon the quality of sounds. Tests show that, below 100 cycles per second, the efficiency is not materially affected by tubing length. Between 100 and 1 000 cycles per second, tubing length exerts a considerable effect: that is, the efficiency decreases with increased tubing length. This efficiency loss occurs in the region of the low intensity high-pitched, diastolic murmurs, and every possible increase in efficiency in this region is of utmost value.

19 In order to obtain the most efficient tubing dimensions, one should make the tubing as short as possible and compromise on the resistance and volume components. The compromise may be approached by plotting a graph representing efficiency versus volume effect, and another representing efficiency versus fric-

tional resistance effect, where the two curves intersect is the point of optimum efficiency

"20. For general clinical use, an electrical amplifying stethoscope must transmit sounds to the observer with a quality and fidelity equal to that of the average acoustic stethoscope. A modification of the frequency response characteristic of an electrical stethoscope will definitely alter the quality and character of the sounds.

"21 An amplifying stethoscope is not primarily an instrument to be used for making sounds many times louder than they can be heard with an acoustic stethoscope. The major advantage of the amplifying stethoscope over the acoustic stethoscope is that it enables one to adjust the intensity to the desired level, and thus eliminate a number of modifying characteristics peculiar to human hearing which cannot be overcome with the acoustic stethoscope.

"22. When filters, either electrical or acoustic, are used with an amplifying stethoscope, they should possess frequency response characteristics similar to those of the various open and diaphragm chest pieces.

"23 For teaching purposes, a loud-speaker may be used in conjunction with the amplifying stethoscope. The over-all frequency response of the loud-speaker and amplifying stethoscope must be identical with that of the average acoustic stethoscope, in order not to modify the quality and character of the sounds.

"24 In order to maintain an identical and known relationship between sounds as heard and as recorded, the recording galvanometer and audiophone must be fed from the same source; that is, the same electrical pulsations which pass to the audiophone are fed into the galvanometer

The 194 paper by Rappaport and Sprague was entitled "The Graphic Registration of the Normal Heart Sounds. *Am. Heart J* 1942, XXII, 591

1 When a patient is auscultated in the usual stethoscopic manner the observer does not hear the cardiac vibrations as they actually exist t the source because of three major forms of modification, namely

a. The heart sounds are altered in their transmission from the source to the surface of the chest.

"b. The heart sounds that reach the surface of the chest are additionally modified by the acoustic stethoscope and the type of chest piece employed.

c The observer does not perceive the heart sound vibrations as they are transmitted to the ears by the acoustic stethoscope.

"2. The three major forms of cardiac sound modification are related to usculta-tion as follows.

a. The chest transmissional factor must be considered and handled as a variable quantity

"b. Modification effects that are introduced by acoustic stethoscopes and their chest pieces may be made non-variable. No attempts at stethoscopic standardization have as yet been made. Until such standarizations are accomplished, the stethoscopic factor must be considered as a variable quantity in auscultation.

c. Modification effects that are introduced by verage normal hearing may be considered as constant quantity in uscultation, with the condition that personal factors, such as auscultatory experience, fatigue, surrounding noise level, and rhythmic concentration ability are omitted.

"3 The three major forms of cardiac sound modification that are encountered in auscultation may have the following relationships to phonocardiography

a. In phonocardiography as in auscultation, the chest factor must be considered as a variable quantity

*b. The modification effects that are introduced by an acoustic stethoscope and its chest pieces in auscultation may be reproduced perfectly by phonocardiography

c. The logarithmic type of modification that is introduced in auscultation by average normal hearing may also be reproduced by phonocardiography

4 Phonocardiographic registration may therefore be considered according to the degree of modification introduced, namely

*a. Linear phonocardiography or the registration of the sound vibrations as they exist on the surface of the chest

*b. Stethoscopic phonocardiography or the registration of the sound vibrations as they are transmitted to the ears by an average acoustic stethoscope.

c. Logarithmic (human audiographic) phonocardiography or the registration of sound vibrations as they are perceived by a competent observer if the personal factors are omitted.

5 Linear stethoscopic, and logarithmic phonocardiography are directly related to auscultation. Each phonocardiographic method is a representation of a definite stage of sound transmission in auscultation. Deviations may be introduced by a phonocardiograph with frequency response characteristics other than linear, stethoscopic, or logarithmic. Such deviations bear no direct relationship to the auscultatory transmission and detection stages. Therefore, a phonocardiograph with other than linear stethoscopic, or logarithmic characteristics must be considered as either an apparatus of poor design or an expression of the designer's personal opinion, unless the deviation is based upon a natural constant.

*6. The linear phonocardiograph is essentially an electrical sphygmograph which possesses several advantageous characteristics not common to the segment capsule or direct optical type of sphygmograph.

*7 A linear phonocardiogram, when registered over the apex, is an "apex cardiogram or apex beat tracing.

*8 A chest piece was devised which makes possible simultaneous phonocardiographic registrations over the same precordial area. For example this dual chest piece is useful for simultaneously registering the apex beat and the stethoscopic or logarithmic phonocardiogram at the apex. Clinically such simultaneous registrations may be useful in differentiating between the third heart sound and the opening snap of the mitral valve when the isometric relaxation phase of the left ventricle is shortened by mitral regurgitation. The apex cardiogram is also useful in timing diastolic events, as in venous pulse registration. In some persons it is rather difficult to record the venous pulse in such cases, the apex cardiogram may be registered instead.

*9 The first heart sound is composed of four components, namely

*a. The first, which is caused by residual vibrations of auricular origin.

*b. The second, which is produced at the beginning of the isometric contraction phase of the cardiac cycle (closure of the mitral and tricuspid valves)

c. The third, which is caused by the opening of the semilunar valves.

d. The fourth, which is caused by the acceleration of the blood in the arterial vessels during the maximum ejection phase of ventricular systole.

10. The linear phonocardiograph is capable of registering the first and fourth

components of the first heart sound efficiently but is very inefficient in the registration of the second and third components.

11 The stethoscopic phonocardiograph registers the first and fourth components of the first heart sound with some attenuation, but does not obliterate the vibrations. The second and third components are registered distinctly

12 The logarithmic phonocardiograph obliterates the first and fourth components of the first heart sound of most normal persons, and registers the second and third components distinctly

13 When a normal person is auscultated, the observer rarely hears the first and fourth components of the first heart sound' the second and third components are well heard. Logarithmic hearing (as indicated by logarithmic phonocardiography) is responsible for this auscultatory condition because of the greater relative attenuation of the low frequency first and fourth components than of the higher frequency second and third components. Logarithmic attenuation of the first and fourth components is of sufficient magnitude to bring them below the level of human audibility

14 A simultaneous stethoscopic or logarithmic phonocardiogram and venous pulse tracing may serve as a means of differentiating between a prolonged first heart sound and a first heart sound which is followed by a short systolic murmur In the latter instance, it extends beyond the c wave peak.

15 Our observations indicate that the second normal heart sound may be composed of four components, namely:

a. The first vibrations, which represent the beginning of the diastolic fall in pressure with ventricular relaxation.

b. The second group of vibrations, which are caused by the closure of the semilunar valves (termination of ventricular systole)

c. The third group, which are most likely due to the arterial wall and blood column vibrations. An additional, possible source of vibration in this phase of the second heart sound may be the natural period vibration of the chest wall, which may conceivably be set into oscillation by the second component.

d. The fourth component is caused by the opening of the mitral and tricuspid valves.

16. The logarithmic phonocardiogram almost always totally obliterates the first, third, and fourth components of the second heart sound vibrations, whereas the stethoscopic and linear phonocardiogram may show all four components. This indicates that no matter how competent an observer may be, he can hear only the second component of the second heart sound of a normal person because his hearing is logarithmic.

17 Although the duration of the normal second heart sound is nearly equal to that of the first, auscultation makes the second sound appear shorter This is explained by the fact that, normally two components are audible in the first heart sound, whereas only one is audible in the second heart sound.

21 For maximum accuracy in all types of phonocardiographic analysis, a phonocardiograph capable of registering the heart sounds linearly stethoscopically and logarithmically should be employed.

Thus it becomes evident that much of the discussion about phonocardiography in the clinic in the past has been unsound because of the failure to

recognize the important differences between the various types of phonocardiograms mentioned above, namely the linear the stethoscopic, and the logarithmic, which not infrequently have been erroneously compared as if they were the same in detail Despite the importance of their distinction it is possible that many of the vibrations that are inaudible but that can be recorded may in their variations eventually prove to have almost as much clinical significance as the heart sounds and murmurs themselves this is for future studies to determine. Figure 12 illustrates two of the three types of phonocardiogram—stethoscopic and logarithmic—in the same case (see below)

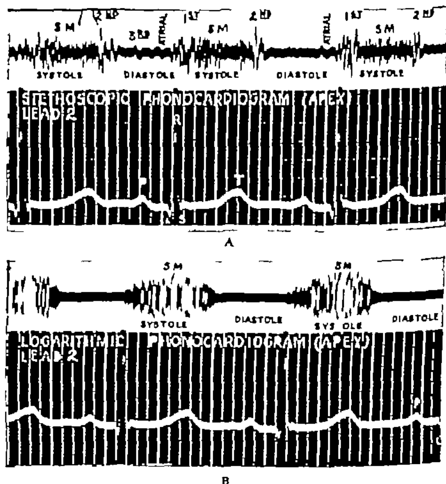


FIG. 12. Comparison of stethoscopic and logarithmic phonocardiograms (*A* and *B* respectively) taken at the cardiac apex in the same individual with loud systolic murmur It is of interest to note in the stethoscopic phonocardiogram the third and the atrial sounds which are not audible to the human ear and are not shown in the logarithmic phonocardiogram also the difference in the records of the murmur is quite obvious. (Kindness of Mr M A. Rappaport, Sanborn Company Cambridge.)

HEART SOUNDS

There are normally three heart sounds but the third is often very faint or even inaudible. The first sound, loudest at the apex, is produced by closure of the mitral and tricuspid valves plus an element of muscular contraction, and roughly marks the beginning of systole at its very beginning and merged with it is a very short presystolic phase due to atrial contraction, which, audible or not, is indistinguishable from the first sound itself unless there is abnormal lengthening of the interval between the atrial and ventricular contractions The second sound, usually loudest at the base in the pulmonary valve area in children and young adults and in the aortic valve area in the middle aged and elderly is produced by closure of the aortic and pulmonary valves, roughly marking the beginning of diastole. The third sound in the normal subject, heard as a rule best at the apex and thence halfway to the left sternal border when it is audible at all, is probably the result of the vibration of the ventricular walls and atrioventricular valve cusps caused by the inrush of blood in every diastole It is best heard in children, after exercise, and in the recumbent position. It occurs early in diastole, about 0 1 second after the second sound. The "opening snap" of the atrioventricular (chiefly the mitral) valves, if heard at all, forms but a late part of the second sound or at most reduplicates it, it comes definitely earlier than the time of the third heart sound.

The heart sounds are proportionately increased in intensity when the chest wall is thin and as the result of increase in blood flow by exercise, excitement, or certain drugs. They are proportionately decreased by a thick chest wall, pulmonary emphysema, and a state of weakness, prostration, or shock.

First heart sound. The first sound is *accentuated* at the apex when the heart action is forceful and the blood flow is rapid, as normally after exercise or excitement and abnormally in thyrotoxicosis and in some cases of neurocirculatory asthenia It is most accentuated in the presence of mitral stenosis with forceful heart action. It is not primarily accentuated at the base, but it may be so at the lower end of the sternum in very rare cases of tricuspid stenosis.

The first sound is *diminished* at the apex and secondarily at the base in the presence of great myocardial weakness and failure and temporarily when there is a *state of vasomotor shock*, approaching then the usually lesser intensity of the second sound at the apex, it gives rise to tic-tac rhythm. Extreme weakness of the first heart sound is a bad sign.

The first sound may be *masked* by a systolic murmur either at apex or base. The most complete obliteration of this sort is by the harsh systolic murmur of aortic stenosis.

The first sound at the apex may be delayed by the hemodynamic conditions that exist in mitral stenosis, occurring a perceptible interval after the beginning of the apex impulse itself (Cosmo, 1943)

Finally the first sound may be *reduplicated*, such reduplication is best heard

at the apex and results from either (1) an asynchronism of the closures of the mitral and tricuspid valves, due to asynchronism of left and right ventricular contractions as in bundle branch block, or to other cause of change in the intraventricular and intra-atrial pressure relations, or (2) a delay in atrioventricular conduction (first grade of heart block) whereby the atrial contraction sound *precedes the first ventricular sound by a small fraction of a* second.

Second heart sound The second sound is not primarily accentuated or diminished at the apex. *Its accentuation* at the aortic valve area with the subject at rest is commonest in cases of systemic hypertension, especially hyperpiesia but it is occasionally louder than normal and metallic in character when there is dilatation of the aorta in syphilitic aortitis and with marked arteriosclerosis. Accentuation of the second sound in the pulmonary valve area may be normally produced by exercise and by deep expiration, particularly if the subject is supine If it is accentuated with the subject at rest and breathing quietly it is a sign of pulmonary hypertension due most commonly to weakness and failure of the left ventricle, occasionally to mitral stenosis, and rarely to acute or chronic obstruction in the pulmonary circulation itself (as in the acute and chronic cor pulmonale—see Chapter 20) or to congenital defects, especially an atrial septal defect. A point of great importance is the relationship between the intensity of the aortic and pulmonary second sounds. In an *older person and in a patient with systemic hypertension without heart failure* the aortic second sound is greater than the pulmonary second sound. When in such individuals the sounds become equal in intensity or the pulmonary second sound becomes the louder we have evidence of pulmonary hypertension, this in the case of systemic hypertension means weakness and failure of the left ventricle Recovery from the heart failure is attended by a return of the intensity of the pulmonary second sound to a level below that of the aortic second sound.

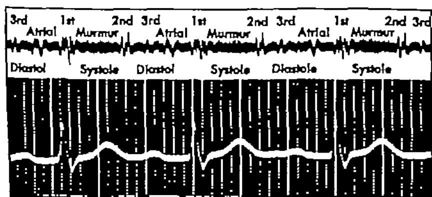
The second sound is primarily *decreased in intensity* to an important degree chiefly at the aortic valve area. This is found particularly with aortic stenosis, when the sound may be entirely absent, and temporarily with a state of vasomotor shock. *With congenital pulmonary valve stenosis the pulmonary second sound may be much diminished or rarely absent.* It is to be observed, however that the second sound heard at either aortic or pulmonary valve area may be transmitted to that point from the other side of the sternum this fact has been inadequately recognized and noted.

The second sound may be *masked* by a loud early diastolic murmur at the aortic valve area and along the left border of the sternum in occasional cases of marked aortic regurgitation

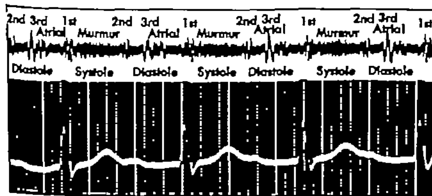
Reduplication of the second heart sound is maximal at the base and is due to asynchronous closure of the aortic and pulmonary valves as the result of a disturbed balance of blood pressure relations between the ventricular cavities on the one hand and the aorta and pulmonary artery on the other hand, or of asynchronous contraction of the ventricles as in bundle branch block. Re-

duplication of the pulmonary second sound is quite common and like the pulmonary systolic murmur may be produced in the normal individual by deep expiration in the supine position. When well marked, with the subject at rest, it is, like accentuation of the pulmonary second sound, suggestive of mitral stenosis. The opening snap of the mitral valve, if accentuated, may reduplicate the second sound at the cardiac apex.

Third heart sound. *Accentuation* of the third sound or the appearance of an extra sound early in diastole (Figure 13) may be caused in slight degree by



A



B

FIG. 13 Stethoscopic phonocardiograms showing in *A* with normal *P-R* interval, normal occurrence of first, second, third, and atrial sounds (and systolic murmur) and in *B* with prolongation of the *P-R* interval in the same case, the superimposition of third and atrial sounds to give summation effect. (Kindness of Mr. M. A. Rappaport, Sanborn Company Cambridge.)

exercise· when marked it is the result of one of three underlying causes (1) most commonly dilatation of either ventricle, (2) mitral stenosis, or (3) delay in atrioventricular conduction so that the atrial contraction sound falls with it to reinforce it. When the third or extra diastolic sound is loud, there

is usually a palpable or even visible extra cardiac impulse accompanying it.

Infrequently one hears an extra sound in systole, a snap or twang shortly after the first sound and heard best at the cardiac apex. It is a curiosity of academic interest only being found as a rule in healthy individuals without heart disease three cases showing this anomaly and diagnosed correctly ante mortem were reported by Huchard (1893) to have had anomalous chordae tendineae that were undoubtedly the cause of the extra sound, an instance of interposition of the atrial contraction in the midsystolic phase has also been noted (Hinohara, 1941)

Gallop rhythm. Gallop rhythm is the descriptive term that has been applied to the auscultatory finding of a well heard extra sound, whether in systole or diastole, when the heart rate is rather fast, that is, 100 or more. Its significance is indicated by the factors responsible for the extra sound as outlined above.

Gallop rhythm is often hard to time but usually it is easy to distinguish between the systolic and diastolic varieties. The former is rare the latter is common. In turn *diastolic* gallop rhythm is divided, when possible, into protodiastolic and presystolic in timing, but often it is impossible, even with graphic records, in the presence of considerable tachycardia to decide which is which, and one has then to be content with the simple designation "diastolic.

Protodiastolic gallop rhythm, that is, the kind with the loud third sound early in diastole, if it can be so timed, when located at the cardiac apex, is *usually a serious sign, since left ventricular dilatation is the commonest* accompaniment of marked accentuation of the third sound. A protodiastolic gallop rhythm may be heard best at or be limited to the precordium just to the left of the mid or lower sternum in such cases great right ventricular strain is usually very evident and the gallop is probably the result of dilatation of the right ventricle

A *presystolic* gallop is less serious than a protodiastolic gallop: it is found when there is slight delay in atrioventricular conduction or in certain cases with very forceful atrial contraction (in chronic hypertension, for example)

A *systolic* gallop is of no clinical importance, although it may be present in heart disease.

In rare cases four heart sounds are heard with each heart cycle, the first, second, and third sounds and a presystolic sound (produced by atrial systole)

Atrial sounds. Atrial contraction when forceful produces a sound or even a double sound which ordinarily forms a part of and is buried in the regular first sound of the heart, when there is delayed conduction or high-grade heart block the atrial sound may be faintly audible at the left border of the sternum or at the apex, best heard with the bell and with the subject supine (Figure 14)

There are two other points of special interest about heart sounds that deserve mention. One of the curious phenomena in medical observation, doubtless dating back to the earliest days of mankind, many centuries before auscultation, either mediate or immediate, is the occasional *audibility of the*

heartbeat at a distance sometimes with the ear but a few inches from the chest wall and sometimes across a wide room. One cause of such audibility is left pneumothorax, another is pneumopericardium and a third is intracardiac and apparently due to rupture of valve cusp, chorda, or lax infarcted papillary muscle which allows the mitral valve to slap shut with great suddenness. Change of body position and of breathing may greatly affect the degree of audibility

The other point concerns the variation in time interval that may occur even

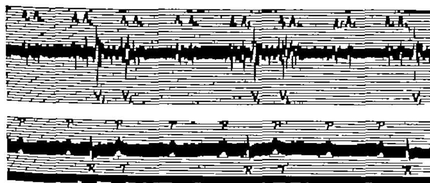


FIG. 14 Phonocardiogram (upper tracing) showing double atrial sounds in complete heart block. Electrocardiogram taken simultaneously is shown below Time interval = 1/30 second. (Lewis *Lectures on the Heart* Kindness of Paul B Hoeber Inc New York)

in successive beats, between the electric and acoustic records of the heart's action, as has been pointed out in two cases of atrial fibrillation (Luisada, 1941) the interval was longer after a short diastole

VASCULAR SOUNDS

In the great vessels at the base of the heart and extending into the neck and below the clavicles, sounds may be heard which are transmitted from the heart. Over the jugular veins, especially over the right-sided jugular bulb three sounds may be faintly heard if the pulsation there is vigorous and atrial contraction active. These three sounds coincide with the three chief waves normally seen in the jugular pulse, the so-called *a*, *c* and *v* waves. The first is due to atrial contraction and the other two sounds are undoubtedly the result of transmission of the usual first and second sounds from the heart. Otherwise the only vascular sound (not murmur) that is audible is that found over any large artery when it is compressed. Under certain conditions no compression is needed to hear this arterial sound occurring with the pulse and due to the sudden tension of the arterial wall these conditions are aortic regurgitation and marked peripheral vasodilatation with vigorous heart action, both of these conditions being responsible for the relative emptiness of the arteries at the end of diastole when the next pulse comes through. Under such

conditions with compression (or even without it) the sound heard over the greater arteries, as over the femoral artery at the groin, may be very sharp and has been called the *arterial pistol shot sound*.

Finally mention may be made of *fetal heart sounds* which undoubtedly were heard with the ear applied to the abdominal wall long before stethoscopes were invented. They are usually faint and so rapid that it may be difficult to distinguish between the first and second heart sounds. They are generally well heard with the bell receiver attached to the binaural stethoscope. Disturbances of rhythm and rate of temporary significance may be noted, and rarely murmurs or arrhythmia of permanent importance, such as congenital heart block, may be found. Little study has as yet been directed to the possibility of diagnosing heart disease from fetal heart sounds, although occasional fetal phonocardiograms have been obtained.

CARDIOVASCULAR MURMURS

Cardiovascular murmurs, like thrills, are produced by the vibration of the valves and walls of the heart and great vessels resulting from the rush of blood from a passage of relatively narrow caliber to one of much greater caliber and by the vibration of a torn or everted valve cusp or of some tissue floating in the blood stream one end of which tissue is fixed to valve or to heart or vessel wall, and quite likely by the effect of certain forceful eddies of the blood in its course through the heart. Considering the sinuous course of the blood stream it is surprising that murmurs are not routinely found over all hearts, whether normal or not, rather than that they occur in only a certain number under basal conditions.

Speed of blood flow is the most important modifying factor If the flow is fast the murmur will be louder if the flow is slow the murmur will become fainter and if the flow is very slow the murmur may disappear altogether. External modifying factors, as in the case of heart sounds, are common these include obesity and emphysema which diminish the loudness of the murmurs, and leanness which increases their loudness. In children murmurs are more easily heard than in adults. The transmission of murmurs in direction and extent depends partly on the loudness of the murmur partly on muscular and bony conduction in contrast to the damping action of air fluid, and fat, and partly on the direction of flow of the responsible blood stream.

Certain other observations about murmurs are of importance before discussing the individual types. Narrowing of a stream of blood without a fairly abrupt dilatation of the caliber of the containing vessel or chamber further on does not cause murmurs. Roughening of the surface of the walls of heart or blood vessels does not cause murmurs unless there are appreciable projections or torn fragments to vibrate in the blood stream. It is the relation between the calibers of two adjoining parts of the heart or blood vessels, and not the absolute size of the caliber of either that determines the production of murmurs. For example, there may be a loud systolic murmur in the second inter-

costal space close to the sternum if the aorta is dilated even though the aortic valve is normal, just as there may be if the aortic valve is stenosed and the aorta of normal caliber Also, even though the mitral valve is normal, there may be an apical diastolic rumble if well-marked dilatation of the left ventricular cavity (with or without aortic regurgitation) is present, just as there may be if the mitral valve is stenosed and the left ventricular chamber is of normal size. The combination of the two factors in either case, that is, valvular stenosis and dilatation of aorta or of left ventricular cavity favors an increase in the murmur which may be caused by either factor alone.

Heart murmurs may be temporary and due to relatively unimportant functional disturbances. It is of great importance to recognize and remember that most systolic murmurs do not indicate the presence of any structural or "organic" heart disease. Nevertheless, serious diagnoses and bad prognoses have frequently been made largely on the basis of such murmurs. On the other hand, it should be recognized that even slight systolic murmurs, except in the pulmonary valve area, may be abnormal they demand study as to their cause. Often they are found to be unimportant "functional" murmurs, but frequently they are evidence of the presence of some important or serious disease acting on the circulatory apparatus even though there be no heart disease itself These facts require the application of study and common sense to the interpretation of murmurs and avoidance of the extreme views, with overemphasis and underemphasis, which have held sway during the swing of the pendulum in the past generation.

At this point I would like to urge a revision of the nomenclature of heart murmurs, following suggestions published by Adams, Craib, and myself (1942) The old time-worn phrases "functional" and organic" as applied to murmurs are highly unsatisfactory for important reasons in each case. "Functional" has been used equally to signify physiologic and pathologic, and even when its interpretation is the latter there is no separation as to extracardiac or intracardiac causation. "Organic" has been in the past limited to structural deformity of a valve, even though there may be present much more serious organic disease of the heart than valvular deformity to cause a murmur which has been labeled "functional. Also it is often impossible to decide, at first at least, whether valvular deformity or cardiac dilatation without valvular disease is responsible for a murmur even though it is obviously pathologic. Therefore we recommend that the terms "functional" and "organic" as applied to murmurs be dropped and the designations "physiologic" and "pathologic" used instead, with proper subdivision of the latter into extracardiac causation, as from anemia, and intracardiac causation, as from myocardial involvement (rheumatic myocarditis, myocardial infarction, or myocardial failure) on the one hand, and valvular deformity (with stenosis, regurgitation, or both) on the other There may of course, be multiple causes for pathologic murmurs in the same case. And in those cases in which we cannot tell whether a murmur is physiologic or pathologic, we should so indicate.

Furthermore, it is of great importance to realize that serious heart disease

(or other diseases) may be present in the absence of all heart murmurs, and even with normal heart sounds in some cases. Hypertensive heart disease, congenital heart disease, the thyroid heart, syphilitic aortitis, and serious coronary disease with or without angina pectoris may be unattended by heart murmurs. Moreover some conditions while slight in extent give rise to marked murmurs and when greater in degree they become murmurless. This may be illustrated by three instances. If mitral regurgitation, "functional" or "organic," is slight in degree with forceful heart action there is likely to be a loud apical systolic murmur due to the small aperture if this mitral regurgitation becomes very extensive with a very large aperture between ventricle and atrium no murmur at all may be found, even though the condition is much worse. If a congenital defect of the ventricular septum is small, as is the rule a loud systolic murmur with thrill characteristic of the condition results, but if the defect is so extreme that the septum is wholly lacking or only rudimentary there is no resultant murmur at all, while the defect is of course far more serious. These facts are easily explained by the first comments made above about murmurs. A third example is in the case of stenosis of aortic or mitral valve with well-marked murmur when heart failure of serious degree sets in, this murmur decreases in intensity and may even disappear in rare cases moreover the presystolic phase of the mitral diastolic murmur disappears when atrial fibrillation replaces normal rhythm.

The intensity of heart murmurs may be very simply and adequately expressed by gradation as follows very slight, slight, moderate, loud, and very loud. This classification may be expressed by the terms *grade 1 grade 2 grade 3 grade 4* and *grade 5* a very useful procedure, as advised by Levine (1933). In addition to notation of the intensity of heart murmurs there should always be a statement as to their exact timing, character (blowing, rumbling, low or high-pitched, etc.) location, and transmission. The terms "constant and "inconstant have no value as applied to heart murmurs to distinguish between pathologic and physiologic types, since some of the former are inconstant and many of the latter are constant.

As is the case with heart sounds, so on rare occasions very intense heart murmurs may be heard without a stethoscope and with the ear at some distance from the chest wall, even the width of a room. Such murmurs, either systolic or diastolic in time, are in the main very loud and high-pitched and are due to unusual valve deformities, especially rupture of cusps or chordae tendineae.

Finally it is to be noted that all murmurs heard over the heart are not intracardiac in origin some are due to the movement of air in the lungs as the mechanical result of cardiac contraction or to the rubbing together of pleural or of pericardial surfaces even though uninflamed.

Systolic murmurs. 1 *At the cardiac apex* (Figure 12, page 30) The systolic murmur heard at the apex of the heart is commonly blowing in character, of moderately high pitch but not as a rule musical, beginning with or immediately following the first sound, and varying from very short in length and slight in intensity so that it is just recognizable as a murmur rather than as an impure

or slurred first sound, to a very long and loud murmur filling all of systole. The louder this murmur the wider is the area over which it may be heard. Transmission of this murmur to a distance is largely based on the two factors of loudness of murmur and nearness of heart to stethoscope, as is true in the case of most murmurs. An apical systolic murmur therefore, which is transmitted to the left axilla, toward the base of the heart, or back of the chest, is in the main a loud murmur This type of apical systolic murmur is due to systolic regurgitation of blood through the mitral valve from ventricle into atrium. This regurgitation may be the result of organi disease (deformity) of the mitral valve, usually rheumatic in origin, but this is the rarest of the three usual causes. It is more commonly due to organic disease of the heart with dilatation without any deformity of the mitral valve. But it is most commonly due to some condition elsewhere in the body which acts by causing a temporary or permanent dilatation of the heart without any real organic cardiac disease or mitral valve deformity such a condition may be either physiologic (if temporary) as after exercise in a rapidly growing child, or pathologic, as in severe anemia. When cardiac dilatation is the cause of the mitral regurgitation and murmur there are two factors to blame, the relative importance of which it is difficult to judge. The ring of attachment of the mitral valve may be stretched so that the valve no longer fits tightly or the ventricular dilatation, by displacing the papillary muscles downward and outward, may prevent the chordae tendineae from stretching sufficiently to allow the valve cusps wholly to close. Furthermore, it is conceivable that some valves which are originally less perfectly constructed, leak with very little provocation. In the case of a deformed mitral valve it is the shortening and fusion of the chordae tendineae, due to inflammation and cicatrization, as well as the defects of the cusps themselves, that allow the regurgitation of the blood stream.

It is not rare for more than one of the three conditions named above causing mitral regurgitation to be present in the same case, as, for example, coronary heart disease with cardiac weakness and dilatation, aggravated by severe anemia.

Another known cause for an apical systolic murmur besides mitral regurgitation, is transmission of a systolic murmur from the base or from under the lower sternal region, such as occurs commonly in cases of aortic stenosis or dilatation, and rarely in cases of interventricular septal defect or pulmonary stenosis. Such a transmitted murmur heard at the apex but maximal elsewhere is far rarer than a systolic murmur maximal and originating at or near the apex. Uncommonly the harsh systolic murmur of aortic stenosis is better heard at the apex than at the aortic valve area itself A point of much value clinically in distinguishing between the systolic murmurs of mitral regurgitation and of aortic stenosis, but relatively slightly known or emphasized, is that a loud apical systolic murmur due to mitral regurgitation is well heard in the lung bases in the back but poorly at the base of the heart or in the neck, while the aortic systolic murmur is poorly heard over the lung bases and well in the neck and at the cardiac apex.

Finally a systolic murmur at the apex is in a few cases obviously due to the movement of air in and out of adjacent or overlying lung tissue caused by the mechanical action of the heartbeat itself or to pericardial or pleural rubbing Cardiac systole may compress lung tissue, especially if it is fixed over the heart at the apex, and squeeze air out, or it may cause a suction of air into lung tissue which had been compressed by the heart in diastole. It is generally, but perhaps not always, possible to differentiate this so-called respiratory systolic murmur from systolic murmurs of intracardiac origin the respiratory character and particularly its variations in different positions of the body and in different phases of respiration (in one of which especially full inspiration, it may disappear entirely) and the relative constancy and quality of the intracardiac murmur usually distinguish between the two Sometimes râles also are produced in the lungs by the action of the heart causing movement of air back and forth through moisture in the bronchioles this association of râle production with heart action may help to explain respiratory murmurs present in the same case. The most common form of cogwheel respiration is respiration punctuated by frequent respiratory murmurs due to the heart's contraction.

It has been shown that the rubbing together of uninflamed pericardial or pleural surfaces can produce murmurs, mostly systolic but sometimes diastolic (Ortiz, 1933) Almost certainly some of the extracardiac murmurs heard clinically are of this origin

There may be other causes for the apical systolic murmur which we do not yet know but certain old terms like "hemic and accidental should be omitted. Anemia, malnutrition, and infections act by causing cardiac dilatation and speeding up the blood flow and so produce pathologic murmurs of extracardiac origin.

The time, intensity and character of an apical systolic murmur and even the presence of a palpable thrill, do not show whether or not the valve is damaged, though the loudest murmurs masking the first sound and accompanied by thrills are more often found with valvular disease than without it. When chronic rheumatic heart disease is present with mitral stenosis the mitral valve lesion may be considered chiefly responsible for the regurgitant murmur and sometimes in young children with a history of recovery from rheumatic fever mitral valve disease may be considered responsible for constant loud apical systolic murmurs even before mitral diastolic murmurs have developed. However is is very important to note that during the acute or subacute rheumatic infection without previous rheumatic attacks both systolic and diastolic murmurs originating at the mitral valve are the result of left ventricular dilatation secondary to the myocardial involvement, and not to mitral valve deformity which takes in all probability at least a year and more likely two or three, to become established sufficiently to cause murmurs (see Chapters 14 and 26)

A word should be added about the time of the apical systolic murmur As a rule the murmur begins early in systole and continues much of the way through if it fills systole it is sometimes called holosystolic. The louder and

harsher the murmur the more likely it is to mask, not really to replace, the first sound. In a few cases it begins at an appreciable interval after the first sound or even in mid or in late systole, such a late murmur is more likely to be of respiratory than of intracardiac origin, but it may be due to the slow yielding in systole of a weak mitral valve ring.

2. *At the base* As in the case of heart sounds, there is a distinction between systolic murmurs heard in the second intercostal space just to the right of the sternum and in the same space just to the left of the sternum. For the sake of convenience these regions have been called the aortic and pulmonary valve areas respectively and they will be so considered here.

(a) *Aortic area.* There are four chief causes for systolic murmurs heard at the aortic area. They are (1) dilatation of the aorta without aneurysm, (2) aortic and subaortic stenosis, (3) aortic aneurysm, (4) transmission of a systolic murmur from pulmonary area, from mid or lower sternum, or even from the apex. The commonest cause of an aortic systolic murmur is simple dilatation of the aorta, whether due to chronic hypertension, the dynamic effect of aortic regurgitation, arteriosclerosis, or syphilitic aortitis. Upward pressure on heart and great vessels by high diaphragm, as in extreme obesity favors the production of an aortic murmur in such cases hypertension is also frequently present. A very important and not infrequent cause of an aortic systolic murmur is aortic stenosis which is most commonly of rheumatic or unknown origin, rarely due to congenital subaortic or aortic ring stenosis, and, in more than slight degree, only occasionally the result primarily of calcareous disease, although calcification is often superimposed on an already damaged aortic valve to increase the degree of its stenosis in the more chronic cases. In the case of congenital subaortic stenosis, that is, of stenosis of the infundibulum or outflow tract of the left ventricle, the loud rough systolic murmur may be better heard in the third right intercostal space, or even over the sternum itself, than in the second space. A murmur transmitted to the aortic area from elsewhere is not rare. One of the least common causes of an aortic systolic murmur is a saccular aneurysm usually of the ascending aorta, or a dissecting aneurysm of the thoracic aorta.

The aortic systolic murmur is generally blowing in character except in aortic stenosis, when it is harsh and rough. It varies in intensity from slight to very loud, the latter intensity usually indicating aortic stenosis, in which condition the murmur may be so intense that it is heard all over the chest, neck, and head, and even in rare cases with the naked ear a few inches from the chest wall. The aortic systolic murmur tends to be transmitted often in its fullest intensity to the cardiac apex itself, along the larger arteries and bones, into the neck, shoulders, arms, and back (especially down the spine) and even along the abdominal aorta the louder it is, the further it is transmitted. With a very loud murmur there is usually a palpable thrill, most marked when the murmur is especially rough, as is often the case with aortic stenosis. The time of onset of the murmur is almost invariably very early and if the murmur is loud and harsh it commonly masks the first sound completely The duration

of the murmur is somewhat variable but usually extends throughout systole, and in the case of aortic stenosis it is frequently followed by no second sound at all.

(b) *Pulmonary area* A systolic murmur at the pulmonary valve area is often found. It is the commonest of all heart murmurs, and if it is absent with the subject in the upright position it can usually be brought out, in the normal individual as well as in the cardiac patient, by the assumption of the supine position, especially in full expiration. Therefore the pulmonary systolic murmur may be considered to be a normal physiologic event unless of considerable intensity in the upright position even then it should be analyzed carefully before being called abnormal. The mechanism of this physiologic murmur is not known, but it is probably associated with a dilatation of the pulmonary artery under increased pulmonary pressure as in full expiration (or best in the Valsalva experiment, which is an attempted forced expiration with the glottis closed) or with a kinking of the artery by change in position, or with other factors which may lead to dilatation. This physiologic pulmonary systolic murmur is blowing in character begins early in systole but does not mask the first sound, extends through most of systole, is as a rule not widely transmitted, and is associated frequently with accentuation or reduplication of the pulmonary second sound physiologically produced in a similar way

Pathologic dilatation of the pulmonary artery is a much less common but far more important cause of a blowing pulmonary systolic murmur (of varying intensity) than is temporary physiologic dilatation. The causes of this pathologic dilatation are (1) pulmonary hypertension most commonly due to failure of the left ventricle but also to mitral stenosis and certain congenital anomalies, serious chronic pulmonary fibrosis and emphysema, and the rare pulmonary endarteritis (2) thyrotoxicosis, which greatly increases the pulmonary blood flow and so dilates the pulmonary artery and (3) rare congenital defects, especially an atrial septal defect with resultant flooding of the pulmonary circulation (see Chapter 13) Here, as in the case of the physiologic increase of pressure in the pulmonary circulation, the pulmonary second sound is often markedly accentuated and may in rare cases be followed by a blowing diastolic murmur which is discussed later in this chapter

Other causes of a pulmonary systolic murmur are rather rare though important. Congenital pulmonary stenosis is as a rule, but not always, accompanied by a loud harsh systolic murmur usually masking the first sound, and by a palpable thrill. Both murmur and thrill are maximal in the second left interspace near the sternum, sometimes a little higher (second rib) and sometimes, if the infundibulum of the right ventricle and not the pulmonary valve is stenosed, a little lower (third rib or third interspace) Such a difference in site of the maximal murmur and thrill may not, however mean a difference in pathologic state. The character time relations, and intensity of the murmur resemble those of aortic stenosis, but the positions differ and the pulmonary stenosis murmur is not so widely transmitted It is sometimes localized to a small area only 2 or 3 cm in diameter but it is usually very well

heard in the lung bases behind. Patency of the ductus arteriosus, particularly in infants, may cause a moderate blowing pulmonary systolic murmur not so intense as that of pulmonary stenosis, and alone not to be interpreted as evidence of such patency A patent ductus arteriosus can be diagnosed by auscultation, however only if there is a continuous "humming top" murmur Aneurysm of the aortic arch or descending aorta may cause rarely a systolic murmur in the pulmonary area, as may also the occasional congenital coarctation of the aorta if well marked, and the extremely rare true aneurysms of the pulmonary artery itself. Finally systolic murmurs from other regions, especially from the aortic area, may be transmitted to the pulmonary area. The fact that the very loud systolic murmurs and pronounced systolic thrills of both aortic stenosis and pulmonary stenosis are sometimes perceived almost equally well on both sides of the sternum, or even best over the sternum itself, makes the differentiation of these two conditions by auscultation alone at times difficult or even impossible the best differentiation by auscultation is by the transmission of the murmurs, that of aortic stenosis being *widely and loudly* transmitted except to the lung bases where it is heard only faintly and that of pulmonary stenosis being transmitted *not far* except to the lung bases.

3 *Elsewhere over the precordium* There are two other areas besides apex and aortic and pulmonary areas where auscultation may reveal maximal sites for systolic murmurs. They are at the lower end of the sternum and in the third and fourth intercostal spaces just to the left of the sternum. Ruling out, in the first place, systolic murmurs transmitted from other areas where they are generally much louder we come to the very rare systolic murmurs originating in these two regions. To the left of the sternum in the third or fourth intercostal space, or in both, a loud blowing systolic murmur may be heard in cases of congenital interventricular septal defect. If such defect is uncomplicated (as is sometimes not the case) such a murmur is called the Roger murmur (and the condition, Roger's disease) A palpable thrill usually accompanies this murmur Pulmonary or more probably infundibular stenosis is a less likely congenital cause for this type and position of murmur Finally a systolic murmur originating under the lower end of the sternum is rare, signifying tricuspid regurgitation with a considerable degree of tricuspid stenosis. Tricuspid regurgitation, which is most often due to dilatation and not to valve damage, is, in contrast to mitral regurgitation, rarely accompanied by murmurs, probably because the tricuspid ring is larger and the right heart chamber pressure differences less. Mitral regurgitation, aortic stenosis, or some congenital cardiac defect, is, by transmission, much more likely than is tricuspid disease to cause a loud systolic murmur at the lower end of the sternum.

4 *Vascular systolic murmurs.* Murmurs, systolic in time, that is, coincident with the appearance of the pulse wave, are common over arteries. At the base of the heart and in the main branches of the aorta three causes exist for their occurrence marked arterial dilatation with or without saccular aneurysms, constriction by internal deformity or pressure from without (with the murmur

found at the end of the constriction where the caliber increases again to normal or beyond) and transmission of a loud murmur from the aortic area as in aortic stenosis. Over the larger peripheral arteries like the brachial, femoral, and popliteal pressure applied artificially from without easily produces systolic murmurs and thrills as is observed routinely in blood pressure studies. Also, compression by tumors, cicatrices, or other causes may give rise to systolic murmurs and thrills, as may large aneurysms with active blood flow. Over the veins isolated systolic murmurs are not found but, as will later be mentioned, continuous murmurs may be present. Over the thyroid gland in exophthalmic goiter a very striking vascular murmur is heard, called a bruit, generally continuous with systolic accentuation and accompanied by a palpable thrill. It is doubtless due to the greatly increased arteriovenous blood flow through the hyperactive gland.

Systolic murmurs may be heard rather easily with either bell or Bowles type of stethoscopic chest piece but as they rise in pitch they are more readily perceived by the Bowles receiver. Certain murmurs are better brought out and are more likely to appear with the subject in one position than in another as, for example, the pulmonary systolic murmur which may be produced by the assumption of the supine position. Finally, one systolic murmur may be superimposed on another, the harsher or louder one predominating, making it very difficult to distinguish the two components.

Diastolic murmurs. Diastolic murmurs are less common but usually more important than systolic murmurs; they have often been called the most serious auscultatory findings, but this is not always so since the careful study of heart sounds and the detection and correct interpretation of certain frequent but neglected systolic murmurs may give us more information about the heart in the long run. Diastolic murmurs are often difficult to hear. It is for their detection that the use of the two stethoscopic chest pieces is so helpful and the examination of the subject in both upright and recumbent positions so important. To test the effect of change in position it is most convenient and generally sufficient to examine the patient first upright and then supine or in the left lateral position. Before proceeding with the special diastolic murmurs of intracardiac origin it should be noted that in diastole, as in systole, though far less often, "respiratory" murmurs may be produced by the action of the heart in squeezing air out of or sucking air into lung tissue, especially if the lung happens to be fixed in close contact with the heart. Such murmurs can be distinguished almost always by their respiratory quality, by the ease with which they are caused to vary or disappear with forced respiration or change in body position, by the fact that they tend to occur at an interval after the second heart sound and not directly with it, frequently by their nearness to the ear, and sometimes by the simultaneous occurrence of pulmonary râles due to the mechanical effect of the heart's action in sucking air in and out through moisture-filled bronchioles. It is quite likely that a few of these so-called respiratory or other extracardiac diastolic murmurs are, like systolic

murmurs, produced by the friction of uninflamed pericardial or pleural sur faces (Ortiz, 1933)

1 *At the apex.* The only two diastolic murmurs heard at the apex with any degree of frequency are those due to mitral stenosis and to aortic regurgitation.

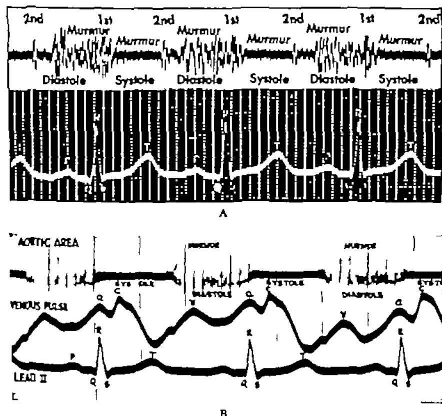


FIG. 15 Phonocardiograms showing the diastolic murmurs of mitral stenosis and of aortic regurgitation. (*A*) Stethoscopic electrocardiogram of classical case of mitral stenosis with very rough mitral diastolic murmur sometimes with presystolic accentuation (note the first beat on the record) Slight systolic murmur also. Observe the interval of relative silence between the second sound and the beginning of the middiastolic murmur f mitral stenosis in comparison with the absence f such an *interval in the case of the aortic diastolic murmur in (B)* (*B*) *Logarithmic* phonocardiogram showing the very musical character of the high-pitched aortic diastolic murmur associated with retroversion of an aortic cusp. Note that systole is clear Simultaneous venous pulse tracing and Lead 2 of the electrocardiogram are recorded. (Kindness of M M. A. Rappaport, Sanborn Company Cambridge.)

These murmurs, unlike superimposed systolic murmurs, are so different that even when they occur together they can be differentiated.

(a) *Organic mitral stenosis* The murmur of mitral stenosis (Figure 15A) has usually five characteristics that distinguish it from the murmur of aortic regurgitation (1) a rough rumbling character generally of low pitch, and

sometimes so low as to be scarcely audible even to a trained ear (2) a failure to appear with or to follow immediately the second heart sound, but instead an onset at a definite interval of time after the second sound, that time interval being the ordinary interval between the second and third sounds of the heart, (3) a localization at the apex, often over a small area of but 2 or 3 cm in diameter with no transmission beyond, a characteristic that not infrequently causes the murmur to be missed entirely unless the examination is very careful and complete, (4) a better perception by the employment of the bell chest piece of the stethoscope than by the employment of other types whose limited use may fail entirely to pick up the murmur when it is not loud, and (5) a better perception with the patient recumbent, the upright position sometimes failing to reveal the murmur even with the use of the bell receiver To these five characteristics may be added five others found less regularly but which are very useful in distinguishing the murmur (6) a palpable thrill localized closely *as a rule, over the apex in diastole, usually somewhat shorter than the* murmur (7) the presence in normal rhythm of a striking accentuation of the murmur in presystole just before or at the beginning of the first sound of the heart, and due to the effect of atrial systole, but absent if atrial fibrillation is present, if the mitral stenosis is relatively slight, or if the atrium is empty or weak when it contracts at the end of a prolonged diastole, (8) the usual presence of an accentuated first heart sound at the apex so often characteristic of mitral stenosis, (9) the common accentuation of the pulmonary second sound, and (10) the frequent presence of a loud third heart sound at the left of the lower end of the sternum or in the space between this area and the apex, and probably due to dilatation of the right ventricle

The murmur of mitral stenosis is explained by the vibration of heart walls and valve caused by the rush of blood through the stenosed mitral valve into the left ventricular cavity Its greatest intensity is usually at its onset at the time of the third sound when the flow of blood into the ventricle begins (which flow does not occur immediately at the time of the second sound, when the aortic valves close at the end of systole) At the onset of the mitral diastolic murmur the flow of blood is, as a rule, faster than at other times because the intra-atrial pressure, with left atrium full of blood, is greatest at such a time in relation to the low intraventricular pressure, which in turn is caused by the passive elastic diastolic ventricular dilatation. The force of the blood stream decreases as diastole proceeds and both murmur and thrill tend to fall off in intensity in diminuendo fashion, to die away entirely if diastole is long (with atrium almost empty and ventricle full) or if the degree of the mitral stenosis is but slight. If normal rhythm exists, there is another increase in the speed of blood flow from atrium to ventricle in presystole due to atrial contraction. If on account of a short diastole (fast heart rate) or marked valvular stenosis, there is still a good deal of blood left in the atrium and still room for more in the ventricle the increase in blood flow through the stenosed mitral valve may be sufficient to cause a final accentuation, variable in degree

and sometimes marked, of the diastolic murmur and thrill just before the first sound, or to make it audible again if it has entirely disappeared.

The presystolic accentuation of the mitral diastolic murmur was formerly described as crescendo in character but the crescendo is actually an auditory illusion, as shown by phonocardiograms and careful auscultation the illusion is due to the combined presence of a sudden accentuation of a murmur that has largely died away and the sharp first heart sound that terminates it. This presystolic part of the murmur of mitral stenosis was at one time considered to be the whole murmur or at least the earliest to appear or the most important or characteristic part. But now we regard it as simply one part of the whole murmur at times striking, to be sure, but often absent as, for example, when there is atrial fibrillation (that is, no orderly forceful atrial contraction) or too slight a degree of mitral stenosis to produce it. If we would rely solely upon the presence of a presystolic murmur for a diagnosis of mitral stenosis we should miss at least half the cases of this valvular lesion. Rarely may a presystolic murmur be present alone, without a middiastolic murmur when the force and speed of blood flow through the stenosed valve happen to be greater in presystole than in middiastole and the degree of stenosis not sufficient to cause a murmur at both times. Careful study of the case should, however be made before recording a diagnosis of mitral stenosis on the basis of what appears to be a presystolic murmur alone without any diastolic rumble or murmur preceding it. Marked accentuation and slurring of the first heart sound such as not infrequently occur in an overactive heart may give a semblance of a slight presystolic murmur and cause an erroneous diagnosis of mitral stenosis to be made, when excitement, exertion, some nervous factor as in neurocirculatory asthenia, or thyrotoxicosis is responsible. If for any reason there is a suspicion of the possible presence of mitral stenosis because of rheumatic history sharp first sound, loud third sound, or unusual heart shape size, or symptoms, and no mitral diastolic murmur is present, exercise (or the administration of a nitrite) may be used as a test to increase the rate of the heart and the speed of blood flow and to bring out a typical diastolic rumble at the apex. Always it is best to examine the subject recumbent after such a test.

Rarely the murmur of mitral stenosis may be a gentle and moderately high-pitched blow following the third sound, but almost invariably it is rumbling in nature and low-pitched when the stenosis is pronounced. An apical systolic murmur of mitral regurgitation may or may not be associated with the diastolic murmur of mitral stenosis. The louder either one of these murmurs, the less intense is the other and if either murmur is marked, the other usually is absent.

Cossio and Berconsky (1943) have pointed out the actual systolic rather than presystolic timing of the very brief vibrations (murmurs) that may precede the delayed and accentuated "first" heart sounds following the shorter diastolic pauses in atrial fibrillation in cases of mitral stenosis.

(b) *Functional mitral stenosis.* There is another fairly common cause of the mitral diastolic murmur besides actual organic mitral stenosis: this is relative mitral stenosis due to considerable dilatation of the left ventricle with the valve normal or not sufficiently damaged to give rise alone to the obstructive diastolic murmur. The clinical conditions in which such relative mitral stenosis is found are chiefly three, namely moderate to severe acute or subacute rheumatic myocarditis, high grades of anemia from any cause, and well-marked aortic regurgitation. In a few scattered cases other causes of left ventricular dilatation are responsible, such as congestive heart failure, but as a rule cardiac dilatation associated with ordinary congestive failure is not attended by a mitral diastolic murmur: in such cases there tends to be a third sound instead. Why this is so is not yet clear but it is probably because the blood flow is not fast enough in these hearts.

In the case of aortic regurgitation various theories have been expressed as to the pathogenesis of the mitral diastolic murmur. It has been generally thought that the blood stream regurgitating through the damaged aortic valve, especially if the posterior cusp is involved, or through the dilated aortic ostium, impinges on the anterior cusp of the mitral valve, thus forcing it back and producing a functional stenosis at a time in diastole when the blood stream is pouring from atrium into ventricle: another theory suggests the production of the murmur by the contact of the two streams from aortic and mitral valves pouring together into the left ventricle, with the anterior cusp of the mitral valve vibrating between them. The best explanation, however, that fits not only the cases of aortic regurgitation but also the cases showing the characteristic murmur with no valve lesion at all is that the left ventricular dilatation is sufficient in degree to give rise to a murmur when the caliber of the blood stream coming through the normal mitral valve suddenly widens out. The time relations, quality, location, and other characteristics of this diastolic murmur of functional mitral stenosis are exactly the same as for organic mitral stenosis except that there is as a rule less intensity to it and usually no associated palpable thrill. When the mitral diastolic murmur is found with aortic regurgitation without mitral stenosis, it has been called the Austin Flint murmur (Flint, 1862).

Flint, Austin. "On Cardiac Murmurs. *Am. J. M. Sc.* 1862, N. S. XLIV. 29

Page 51. As a rule the force of the mitral direct current is not sufficient to develop a murmur unless there be mitral contraction. Is this murmur ever produced without any mitral lesions? One would *a priori* suppose the answer to this question to be in the negative. Clinical observation, however, shows that the question is to be answered in the affirmative. I have met with two cases in which a well marked mitral direct murmur existed, and after death in one of the cases no mitral lesions were found, in the other case the lesion was insignificant. I will proceed to give an account of these cases, and then endeavor to explain the occurrence of the murmur.

A mitral direct murmur, then, may exist without mitral contraction and with-

out any mitral lesions, provided there be aortic lesions involving considerable aortic regurgitation. This murmur by no means accompanies aortic regurgitant lesions as a rule· we meet with an aortic regurgitant murmur frequently when not accompanied by the mitral direct murmur The circumstances which may be required to develop functionally the latter murmur in addition to the murmur of aortic regurgitation, remain to be ascertained. *Probably enlargement of the left ventricle is one condition.* [Italics mine.]

(c) *Transmitted murmurs* Other diastolic murmurs that may be heard at the apex are transmitted from elsewhere. They are due to aortic regurgitation frequently to the very rare pulmonary regurgitation seldom, and to tricuspid stenosis probably not at all, the murmur in this last-named condition not being distinguishable at the apex, if it could be heard there, from the murmur of mitral stenosis which is almost always much more prominent in such cases.

2. *Diastolic murmurs at the base* In the case of basal diastolic murmurs the differentiation of sites is not so important as in the case of basal systolic murmurs, since the two diastolic murmurs found are both heard maximally often in the same place, and have the same characteristics. Other data, therefore, than site and characteristics must generally be employed to differentiate them, the most important point is that the murmur of aortic regurgitation is far more common than that of pulmonary regurgitation.

(a) *Aortic regurgitation* (Figure 15B) The auscultatory characteristics that distinguish aortic regurgitation from mitral stenosis and tricuspid stenosis, but not from pulmonary regurgitation, are (1) a blowing, rarely musical, quality either high- or low-pitched, often very gentle (2) an onset with, or at once after the second heart sound, the murmur if intense completely masking the sound (3) a maximal audibility over the midsternum and immediately to the left of it, in the third and fourth intercostal spaces, usually with wide transmission to the apex and left axilla and upward less loudly toward the neck; (4) a better perception with the Bowles type of stethoscopic chest piece than with the bell, although rarely certain lower pitched aortic diastolic murmurs may be better heard with the bell, or even with the naked ear· and (5) a better perception, as a rule, with the patient upright and leaning forward than recumbent. In addition, (6) a diastolic thrill is rarely felt accompanying this murmur· (7) the murmur continues usually through all or most of diastole, decreasing in intensity and never showing a presystolic accentuation (8) the first heart sound is not accentuated, in fact frequently both heart sounds are masked by murmurs and (9) an accentuated third heart sound is not usually found. Very often, particularly if the diastolic murmur is marked, there is also an aortic systolic murmur due either to aortic dilatation or to aortic valve stenosis, but in the latter case, as in mitral valve disease, the louder one murmur becomes, the less loud is the other that is, the greater the stenosis the less the regurgitation and vice versa. It is common in aortic syphilis with aortic dilatation and regurgitation for both systolic and diastolic murmurs to be loud all over the cardiac area including the second intercostal space just to the right of the sternum with both heart sounds masked by them.

The clinical conditions responsible for the aortic regurgitant diastolic murmur are firstly and much more frequently organic aortic valve disease due to rheumatic infection, syphilitic aortic involvement, or sclerotic change, and secondly dilatation of the aortic valve ostium without disease of the cusps themselves due occasionally to syphilitic aortitis, and rarely to chronic hypertension, sclerotic change, senile ectasia dissecting aortic aneurysm, or severe anemia. There is a very interesting variation of the aortic diastolic murmur, more commonly found in syphilitic aortitis than in other conditions, consisting of a very loud high pitched musical character with thrill, and due apparently to eventration of one of the valve cusps (Bellet, et al., 1939 Nichols, 1940) (see Figure 15B)

Uncommonly the aortic diastolic murmur is heard better in the aortic area, that is, in the second interspace just to the right of the sternum than it is along the left sternal border whither it generally is transmitted in maximal degree. Such a maximal localization of the murmur in the aortic area is occasionally found in aortic regurgitation associated with marked aortic dilatation due to syphilitic aortitis when the ascending aorta extends further to the right and upward than normally or when, along with the aortic valve, the ascending aorta is displaced upward and to the right by a very large heart. Also, rarely the aortic diastolic murmur is heard better at the cardiac apex or at the lower end of sternum, or between these sites, than along the left border of the sternum if so, it can easily be distinguished from the mitral (or tricuspid) diastolic murmur by its other characteristics, described above. Often the diastolic murmurs of aortic regurgitation and of organic or functional mitral stenosis occur together at the apex and can be readily distinguished. Finally it should be stated that the diastolic murmur of aortic regurgitation may be found without any peripheral vascular signs this occurs in the lesser degrees of the valve defect; if peripheral vascular signs like the water hammer or capillary pulse are awaited before aortic regurgitation is diagnosed, half the cases of this valve lesion will be missed.

(b) *Pulmonary regurgitation.* Rare, but almost exactly similar in its characteristics to the diastolic murmur of aortic regurgitation is that due to regurgitation through the pulmonary valve The resemblance may be so nearly complete that a distinction cannot be made by auscultation alone. Rarely however does the pulmonary diastolic murmur ever reach in intensity the loudness frequently found in the case of the aortic diastolic murmur When it is unusually marked it is louder in the second left interspace (pulmonary valve area) than it is in the third and fourth interspaces and follows a much accentuated pulmonary second sound these are important clues. In cases with well-marked pulmonary diastolic murmurs there may also be other telltale signs, namely abnormal visible or palpable pulsation in the pulmonary valve area, a loud pulmonary systolic murmur water-hammer pulsation in the pulmonary artery and "dance" of the lung hiluses seen by roentgen ray and abnormal right axis deviation by electrocardiogram. Usually the pulmonary diastolic murmur is not transmitted so widely as is the aortic. With a loud

blowing diastolic murmur along the left sternal border well-marked peripheral vascular signs, such as the water hammer and capillary pulse, are present if the murmur is due to aortic regurgitation and absent if it is due to pulmonary regurgitation this does not apply if the murmur is slight or moderate. Percussion and roentgenologic and electrocardiographic studies are especially helpful in the differentiation between aortic and pulmonary regurgitation. The clinical conditions underlying pulmonary regurgitation are most commonly (1) mitral stenosis causing increased pressure in the pulmonary circulation and dilatation of the pulmonary artery and valve ring without damage to the valve and rarely the remaining causes (2) chronic failure of the left ventricle with pulmonary vascular congestion and hypertension, (3) chronic lung disease giving rise to the same mechanical conditions, (4) chronic obliterating pulmonary endarteritis, (5) congenital defect of the atrial septum with consequent flooding of the pulmonary circulation, (6) congenital defect of the pulmonary valve giving rise to regurgitation, (7) perhaps wide patency of the ductus arteriosus, and (8) acute or chronic endocarditis of the pulmonary valve itself. If mitral stenosis is the underlying clinical cause of the functional pulmonary regurgitation, the diastolic murmur resulting is called the Graham Steell murmur (Steell, 1881 1888)

Steell, Graham. *Physical Signs of Cardiac Disease* Edinburgh, 1881 2nd ed., page 43

Dr Balfour states that diastolic murmur due to mitral stenosis may be audible and have its maximal intensity in the pulmonary area. This murmur is soft and blowing, unlike the apex true diastolic murmur of mitral stenosis, and is probably produced in the pulmonary artery and infundibulum of the right ventricle as a murmur of high pressure, the pulmonary artery being dilated, and its valves permitting of a certain amount of regurgitation. This murmur is not usually constant, at least when first developed. (See also *M Chronicle* Manchester December 1888, "The Murmur of High-Pressure in the Pulmonary Artery)

3 *Elsewhere over the precordium* the diastolic murmurs heard are those already described, transmitted there, except for one very rare murmur heard maximally and often solely over the lower end of the sternum. This exception is the diastolic murmur of *tricuspid stenosis*. In every characteristic except that of position it is similar to the mitral diastolic murmur but it is usually less intense and may have more of a blowing nature. In only extremely rare instances is it heard without an equally loud or louder mitral diastolic murmur and since sometimes the latter murmur is transmitted away from the apex and is heard at the lower end of the sternum a diagnosis of tricuspid stenosis by auscultation is rarely justified. It may be suscepted if the typical diastolic murmur is louder over the lower end of the sternum than elsewhere over the precordium. The presence of a palpable diastolic thrill localized at the same place or much more marked there than at the apex supports the diagnosis of tricuspid stenosis. Other signs obtained by roentgen ray and general physical

examination are important. The underlying clinical condition is organic tricuspid stenosis due to chronic rheumatic endocarditis.

Functional tricuspid stenosis had not been described before I encountered several cases which I believed to be such, with well-localized mid-diastolic murmurs near the lower end of the sternum mitral diastolic murmurs at the apex, and loud pulmonary diastolic murmurs autopsy of one of the cases showed mitral stenosis, obstructing thrombi in left atrium and pulmonary vessels, and marked dilatation of pulmonary artery and right ventricle with no organic disease of pulmonary aortic, or tricuspid valves. This I reported in the third edition of this book in 1944 and have confirmed since.

4 *Vascular diastolic murmurs* Vascular diastolic murmurs are rare. Over the great vessels at the base of the heart there may be transmitted for a short distance a diastolic murmur originating in the heart, but this is far less common or marked than in the case of systolic murmurs. Otherwise there is only the diastolic murmur produced in cases of aortic regurgitation or marked peripheral vasodilatation by the application of moderate to marked pressure over the larger arteries (best over femoral or brachial artery) First there appears the pistol shot sound and systolic murmur and then as the pressure is increased a slight to moderate blowing diastolic murmur is also heard (not a continuous murmur) The appearance of such a murmur is called Duroziez's sign (Duroziez, 1861) The differentiation of the two causes of the murmur has been pointed out by Blumgart and Ernstene (1933) who showed that pressure with the distal and not proximal edge of the auscultatory bell will produce the murmur if aortic regurgitation is the factor responsible, while the reverse is true in cases of peripheral vasodilatation, in accord with the direction of blood flow and mechanism of murmur production discussed above.

Continuous murmurs. There is no continuous murmur of cardiac origin, but there are three of vascular origin and all three of these may be heard over the region of the heart.

1 Probably the most common and certainly the least important cause of such a continuous murmur is the mechanism giving rise to what has been called the *venous hum in the neck* with the subject seated or standing. This murmur of humming character is loudest at the right side of the base of the neck and much less loud on the left side. It is much increased by bending and turning the head to the left, putting the blood vessels on the right side of the neck on the stretch. It is easily and quickly obliterated by light pressure on the neck over the jugular veins sufficient to stop temporarily the downward flow of blood, or by the assumption of the recumbent position—very simple pathognomonic tests. It is a frequent finding in normal individuals, especially children It is not evidence of any disease or pathologic state. It is probably due to the rapid flow of blood (in the absence of all stasis) through the jugular veins into the jugular bulb and on into the superior vena cava. Its importance, so far as the heart is concerned, is that it is frequently transmitted downward over the base of the heart, even close to the lower end of the sternum, and may give rise to such erroneous diagnoses as patency of the

ductus arteriosus and even aortic regurgitation if the diastolic phase of the hum happens to be prominent. Such mistakes have been made in the past and since many physicians are unaware that there even exists such a phenomenon it behooves all examiners first to know that it does exist and then to exclude it before making a diagnosis of cardiovascular pathologic conditions. Lian (1937) has also referred to the probability that rapid blood flow in the superior vena cava may be rarely responsible for a continuous murmur heard along the right sternal border

Brief mention should also be made of the umbilical venous hum heard in some cases of cirrhosis of the liver and in the case of certain congenital venous defects and called the Cruveilhier Baumgarten syndrome (Blain and Clapper 1945)

2. *Patency of the ductus arteriosus* A continuous murmur often with systolic accentuation, heard best and sometimes only in the first or second interspace to the left of the sternum, a little farther out than the site of the pulmonary systolic murmur and faintly or not at all in the neck, is a characteristic sign of patency of the ductus arteriosus. If patency of the ductus complicates congenital dextrocardia or a right aortic arch the continuous murmur is heard at the right border of the upper sternum. This congenital defect may rarely occur however without murmurs or with but a slight to moderate systolic murmur in infancy or when the patent ductus is of very wide caliber If we can exclude the venous hum in the neck and arteriovenous aneurysms, this typical mill wheel, "humming top machinery or "tunnel" murmur is pathognomonic of patency of the ductus arteriosus and can usually be confirmed by other findings. The murmur may be transmitted to other parts of the precordium, though usually it is not, and it may be localized so high in the left side of the chest that it is missed on hasty or careless examination. Its discovery is generally striking and may occasion undue alarm in the mind of an inexperienced examiner There may or may not be a continuous palpable thrill associated with it, there usually is such a thrill if the murmur is intense.

A very interesting new continuous murmur is that produced by the surgical treatment of the tetralogy of Fallot (see Chapter 13) here the subclavian- (or innominate) pulmonary artery anastomosis produces a patent ductus-like murmur on whichever side of the sternum the procedure is carried out.

3 *Arteriovenous aneurysm.* A continuous murmur usually with some accentuation in systole and attended by a thrill, is found on auscultation over any direct arteriovenous connection, sometimes called an arteriovenous aneurysm, wherever it may be whether in the great vessels at the base of the heart (very rare occurrence) in the lungs, in the head or neck, or in the extremities (the most common site) Its interpretation is generally easy Such aneurysm is, as a rule, traumatic in origin, by bullet, shrapnel, knife, or even surgical accident (Linton and White, 1945) It may be congenital (see Chapter 28)

Appearing abruptly at the left upper border of the sternum in a middle

aged or older individual with syphilitic aortitis a continuous murmur is to be interpreted as the result of rupture of aortic aneurysm into the pulmonary artery a very rare and serious event but one which may be compatible with some weeks or months of survival. Correct antemortem diagnosis is possible even though the murmur exactly resembles that of patency of the ductus arteriosus.

4 *Arterial aneurysm.* A rare cause of a continuous murmur is an arterial aneurysm which may involve the aorta, one of its major branches, or a peripheral vessel, usually over such a lesion if a murmur is heard at all it is only systolic in time, but there are conditions such as wide-open unthrombosed cavity with rapid blood flow when the murmur continues into diastole.

5 *Coarctation of the aorta.* Finally in some cases of congenital coarctation of the aorta a continuous murmur of slight to moderate intensity and not continuing throughout all diastole can be well heard over the thoracic spine.

PERICARDIAL FRICTION RUB

Finally in cardiac auscultation we should observe the presence or absence of friction sounds due to acute pericarditis. Such sounds vary from a soft, almost blowing character to extremely rough, loud, rasping, and leathery sounds. Usually they are found in both systole and diastole, and tend to be somewhat louder in systole. They may occur in systole alone, which fact adds to the difficulty of their differentiation from systolic murmurs. The most common site is near the sternum especially along the left edge, but they may be found anywhere or everywhere over the precordium, and if loud enough they may be widely transmitted to the back and elsewhere. If marked, they are attended by palpable thrills. It is often difficult in the presence of pericardial friction sounds to recognize the characteristics or even the existence of heart murmurs masked by them, and if the friction sounds are of unusually soft character it may sometimes be difficult to distinguish them from murmurs. Repeated and daily observations to note the variation and gradual increase or disappearance of such friction sounds may prove necessary for their interpretation and for the diagnosis of underlying valvular or other cardiac disease.

Pericardial friction rubs are almost invariably indicative of acute pericarditis but there are occasional exceptions, as pointed out by Ortiz (1933) when pericardial friction sounds or murmurs may be produced by normal pericardial surfaces rubbing against each other under unusual pressure, particularly in the pulmonary valve area, as in cases of pulmonary artery dilatation in thyrotoxicosis (Goodall, 1920 Lerman and Means, 1933) and of acute cor pulmonale due to pulmonary embolism (McGinn and White, 1935)

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SEE ALSO REFERENCES UNDER GENERAL REFERENCES FOLLOWING CHAPTER 2

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CHAPTER 6

SPHYGMOMANOMETRY NORMAL AND ABNORMAL BLOOD PRESSURE

Hales, S. *Statistical Essays. Containing Haemostaticks or an Account of some Hydraulic and Hydrostatical Experiments Made on the Blood and Blood-Vessels of Animals* W Innys and R. Manby London, 1733 Vol. 2.

Page 1 1 In *December* I caused a Mare to be tied down alive on her Back, she was fourteen Hands high, and about fourteen Years of Age, had a Fistula on her Withers, was neither very lean, nor yet lusty Having laid open the left crural Artery about three Inches from her Belly I inserted into it a brass Pipe whose Bore was one sixth of an Inch in Diameter and to that, by means of another brass Pipe which was fitly adapted to it, I fixed a glass Tube, of nearly the same Diameter which was nine Feet in Length Then untying the Ligature on the Artery the Blood rose in the Tube eight Feet three Inches perpendicular above the Level of the left Ventricle of the heart. But it did not attain to its full Height at once; rushed up about half way in an Instant, and afterwards gradually at each Pulse twelve, eight, six, four two and sometimes one Inch When it was at its full Height, it would rise and fall at and after each Pulse two, three, or four Inches, and sometimes it would fall twelve or fourteen Inches, and have there for a time the same Vibrations up and down at and after each Pulse, as it had, when it was at its full Height; to which it would rise again, after forty or fifty Pulses."

Hales pioneered in the estimation of venous pressure also. On page 13 he wrote as follows

1 In *December* I laid a common Field Gate on the Ground, with some Straw upon it, on which a white Mare was cast on her right side, and in that Posture bound fast to the Gate she was fourteen Hands and three Inches high lean, tho not to a great Degree, and about ten or twelve years old. This and the above-mentioned Horse and Mare were to have been killed, as being unfit for service.

"2. Then laying open the left Jugular Vein, I fixed to that part of it which comes from the Head, a glass Tube, which was four Feet, and two Inches long.

3 The Blood rose in it, in three or four Seconds of Time, about a Foot, and then was stationary for two or three Seconds, then in three or four Seconds more it rose sometimes gradually and sometimes with an unequally accelerated motion

ine Inches more, on small Strainings of the Mare Then upon greater Strainings rose about a Yard, and would subside five or six Inches.

Sphygmomanometry (σφυγμός pulsation, μανός, thin or rare—rarity or tension—and μέτρον measure) consists of measurement of the arterial blood pressure. It is a special method of cardiovascular study which, through its introduction as a routine part of physical examination during the past generation, has revealed the cause of much cardiac enlargement and failure that was previously obscure.

Two centuries or more ago and again one hundred years later actual determinations of the blood pressure of animals were made by the insertion of tubes into arteries to measure the height first, to which the blood column ascended (Hales, 1733) and second, to which it forced a mercury column (Poiseuille, 1828) but the study was applied only to animals in experimental work until much later However long before the development of a satisfactory clinical sphygmomanometer rough attempts were made to estimate human blood pressure by measuring the weight or force needed when attached to a sphygmograph to obliterate the radial pulse (Vierordt, 1855) There followed gradually the methods of pressure application by plethysmograph to the hand (Marey 1876) later by pelottes to the radial artery (von Basch, 1881) and then to the brachial artery and, finally by small and then larger fluid-filled cuffs applied to finger or arm (Riva Rocci 1891) At last came the introduction of the present, comfortable, wide, air filled cuffs for application to the upper arm and to the leg.

Arterial blood pressure in man is read off for convenience in millimeters of mercury instead of in centimeters of water (which would require a measuring tube over 13 times longer) The gauge is either a carefully graduated and calibrated tube of mercury or a spring pressure device with dial and needle (von Basch, 1887) There are today many different models and makes of sphygmomanometers some of these are more convenient, more accurate, or better made than others, but most of them are satisfactory provided they are checked for accuracy Errors may creep into the use of any type of sphygmomanometer too airtight a seal of a tube containing a mercury column may for example, by air compression or by relative vacuum result in errors in blood pressure readings, too low during inflation of the cuff and too high during decompression, completely to nullify the generally reputed greater accuracy of the mercurial sphygmomanometer A maximal error of 3 mm of mercury may be considered permissible for sphygmomanometers in routine clinical use at pressures up to 300 mm of mercury the average error should be considerably less, but great accuracy is not needed clinically since the significance of variations of a few millimeters of blood pressure is generally negligible.

Special sphygmomanometers have been devised for special purposes, such as the recording sphygmomanometers which take graphic records of value

where objective data are desired for a permanent file, and the oscillometer which shows at different pressure levels the fullness of the pulse in a quantitative way The latter is especially useful in studying the peripheral circulation when there is vascular disease or obstruction. A useful new instrument introduced to register the blood pressure in the pulmonary artery and its branches, the right ventricle, the right atrium, and the great veins during cardiac catheterization is an electromanometer devised especially for this purpose, superseding the Hamilton manometer There are various instruments and methods for the study of the venous blood pressure dependent on (1) the force applied by a pelotte (with manometer) to stop the venous flow (2) the amount of air pressure under a glass capsule, measured in centimeters of water necessary to cause collapse of a vein of moderate size, usually on the back of the hand or forearm (von Recklinghausen, 1906 Hooker and Eyster 1908) (3) the height above the level of the right atrium in centimeters to which the forearm and hand are raised before the veins collapse (Frey 1902 Gaertner 1903) and, the most satisfactory method (4) the direct reading of the pressure in centimeters of blood or of sterile normal salt solution in manometer tube connected with a needle introduced into an elbow vein at the level of the right atrium (Moritz and Tabora, 1910 Griffith, et al 1934 Holt, 1940) A method for the graphic registration of the venous blood pressure has also been devised (Kendrew 1926) Finally methods for determining the capillary blood pressure have been introduced, including (1) macroscopic blanching of the skin by pressure under a transparent capsule, a method which is unsatisfactory because it includes the pressure in the smaller arterioles and venules as well, (2) the more accurate microscopic method of direct observation of the blood flow in the capillaries (Lombard, 1912) and, most accurate of all, (3) direct registration of pressure by the introduction of a fine pipette into a capillary (Landis, 1930 Eichna and Bordley 1939)

The systemic blood pressure cannot be estimated by palpation alone with enough accuracy to warrant any confidence in such a procedure. Instrumental sphygmomanometry is essential. There are three technics, which as a matter of fact may be combined for the sake of greater accuracy

The best method of clinical sphygmomanometry is the *auscultation* technic which records systolic and diastolic pressures in most cases very slightly below the actual levels as determined by direct readings from within the artery The systolic pressure is to be read at the point when the first clear sound appears during slow decompression of the blood pressure cuff faint sounds due to the impact of a forceful pulsation against the closed end of the artery at the upper edge of the cuff may sometimes be transmitted to the stethoscope placed over the artery at or just below the lower edge of the cuff at any pressure above the systolic, but these should be ignored. The diastolic pressure should be recorded at the point when the sound abruptly disappears or abruptly drops in intensity rarely the sound continues loudly to zero and the diastolic pressure must be so recorded, as in some cases of marked aortic

regurgitation. In 1939 a joint report was published by committees appointed by the American Heart Association and by the Cardiac Society of Great Britain and Ireland for the standardization of blood pressure readings, in which there appeared a note of difference of opinion relative to a record of the diastolic pressure the American committee recommended that both the level at which the auscultatory sounds become dulled and that at which they disappear (if there is a difference) should be recorded, thus 140/80-70 or 140/70-0 or 140/70-70 while the British committee believed that except in aortic regurgitation it is nearly always possible to decide the point at which the change comes (either abrupt dulling or complete disappearance) and that this is the only reading that should be recorded. A report by a new committee of the American Heart Association in 1951 states that "it appears that the point of complete cessation is the best index of diastolic pressure."

There is no practical value in attempting to record the various auscultatory phases of the pulse pressure, that is, in the interval between the systolic and diastolic levels, except in one respect to be recounted below· usually the upper most phase is one of sound, the second phase which lasts normally over an interval of about 20 or 30 mm of mercury is one of murmur the third phase is one of sound again, and occasionally there is a short fourth phase of diminished sound before the level of silence is reached below the diastolic pressure. The one auscultatory phase that is of special importance and of practical interest is that related to the so-called *auscultatory gap* In occasional cases the murmur phase may be largely or wholly absent, leaving a gap of absolute or relative silence in the middle or upper part of the pulse pressure range. Such a finding is most frequent in chronic hypertension, aortic stenosis, and marked local arteriosclerosis its exact mechanism is not clear An example of such an auscultatory gap is one of 35 mm ranging from 180 to 145 in a patient with systolic pressure of 210 and diastolic of 105 To avoid an important error in such a patient it is necessary to raise the compression of the cuff far enough above this gap so that the true systolic sounds can be heard on decompression, or to check the method by either or both of the other two methods of sphygmomanometry· one can easily carry out both these procedures. If the auscultatory gap is not recognized there may be recorded a systolic pressure as much as 50 mm or more below what it actually is. There are still other sources of error in auscultatory sphygmomanometry too low a reading when the arm is especially small and too high when the arm is very large, but these errors are not great (Bordley and Ragan, 1941) and in general the method is an unusually accurate bedside procedure as checked by direct intra-arterial readings (Steele 1942)

A second method of sphygmomanometry the *oscillatory* is, theoretically more accurate than the other technics but actually less practical because of the frequent difficulty in making the readings. The systolic pressure is the point of abrupt increase in amplitude of the oscillations of the mercury column or needle of the manometer above the baseline of small pulse movements, while the diastolic pressure is the first point of distinct decrease below

the maximal oscillations unfortunately however both these points may be poorly marked because of the failure of any abrupt changes. The method may be carried out visually or by a recording device (Figure 16) Its greatest value is its service as a check on the accuracy of the more practical auscultatory method except in the study of obstructive arterial disease in the extremities, when it has been found that the form of the oscillographic curve is of some importance in determining variations from the normal in the vascular tree and apparently in determining the type of arteriosclerosis (Friedlander 1935).

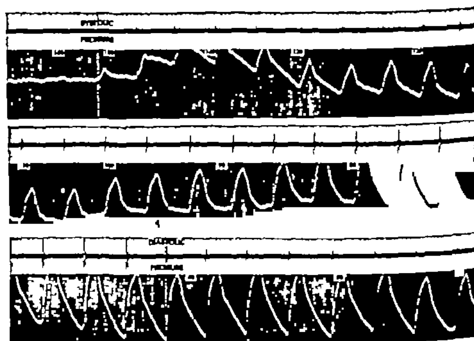


FIG. 16. Human arterial blood pressure record determined by simultaneous brachial arterial tracing and phonogram at systolic pressure of 150 and diastolic pressure of 62. The first definite upstroke of the arteriogram occurs just prior to the record of the first sound. The disappearance of the truncated dip of the arterial tracing occurs at the time of the last well-marked sound record. (Kindness of Mr M A Rappaport, Sanborn Company Cambridge.)

The third method of sphygmomanometry is *palpatory* The point at which the radial pulse is first felt on decompression of the brachial cuff is recorded as the systolic pressure but this is invariably too low by about 5 to 10 mm. The method serves, however as a rough check on the other methods outlined above. The diastolic pressure cannot easily be recorded by palpation, and this explains why in the early days of sphygmomanometry only the systolic blood pressure was measured. Segall, however a decade ago (1940) called attention to the possibility of palpating over the brachial artery the vibrations set up during the pulse pressure interval which correspond to the sounds and murmurs heard by the auscultatory method between systole and diastole.

It is of academic interest that the subject himself can roughly note the levels of systolic and diastolic blood pressure in the arm by the sensations during decompression of the cuff a thrill is felt subjectively just below the systolic pressure level and disappears just above the diastolic level.

Finally there has been a revival, for certain special studies, of the old time direct arterial blood pressure by arterial puncture in man (Wolf and Kindler 1934) and there have been introduced in recent years methods of recording by cardiac catheterization the actual pressures in right atrium, right ventricle, and pulmonary artery and its branches, an especially important development (Cournand, et al. 1944 Dexter et al., 1947)

Systemic arterial blood pressure. The blood pressure in the brachial artery of a normal adult ranges from 95 to 145 mm of mercury *systolic* depending on conditions at the time of the sphygmomanometry Age has some effect on blood pressure, as recently confirmed by Master (1950) There tends to be an increase, though often irregular in systolic pressure of ½ to 1 mm a year Thus at twenty years the systolic blood pressure normally may be 110 mm, at thirty in the same person 115 at sixty 150 and so on. Factors of excitement, exercise, eating, smoking, and fatigue all play a considerable role in many persons, tending to elevate the systolic blood pressure moderately Nervous tension is the factor that influences blood pressure most, elevating it in both normal and hypertensive individuals, but especially in the latter Ayman and Goldshine (1940) found for example that in a series of hypertensive individuals 30 per cent registered a systolic pressure 40 mm or more higher in the clinic than at home and 24 per cent a diastolic pressure 20 mm or more higher. The temporary hypertension that is found in many nervous but otherwise normal young men at the time of examination for athletic sports, military service, or insurance is well known, in fact it is so common that routine blood pressure determination for admission to the army was at one time even considered inadvisable. Figure 17 illustrates the wide range of the normal brachial blood pressure.

The pressure varies also slightly with the respiratory phase but this is unimportant unless the respiration is greatly disturbed or the heart constricted by acute or chronic pericarditis when the pulse may become markedly *paradoxical* (see Chapter 27) the paradoxical pulse consists of marked decrease of the systolic and pulse pressures, even to the point of obliteration, during *inspiration*, in contrast to the usual and normal increase of the pulse during inspiration in the case of diaphragmatic breathing.

In the early morning before arising the systolic brachial arterial pressure may be 105 mm while in the same person in the midst of a busy day it may register as much as 140· strenuous exercise may send it up to nearly 200

The most important and commonest cause of abnormal high systolic blood pressure is hyperpiesia (essential or arterial hypertension) less common causes are nephritis, obstruction to the renal circulation (Goldblatt, 1934) convulsive seizures, brain tumor tumor of the adrenal medulla (pheochromocytoma) and coarctation of the aorta (see Chapter 19) The causes of ab-

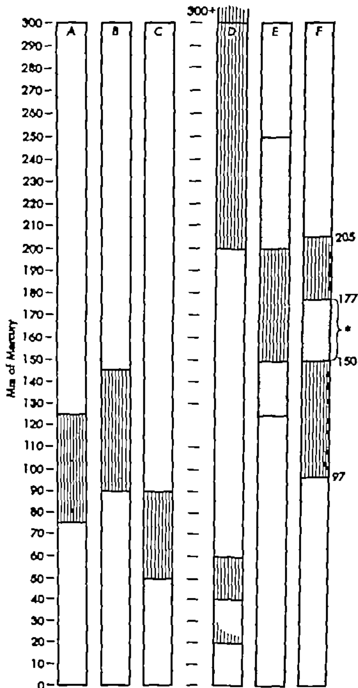


FIG. 17 Diagram showing (*A*) the verage normal ad lt blood pressure (125 mm mercury systolic and 75 diastolic) (*B*) the usual upper limits of normal pressure; (*C*) the lower limits of normal pressure (*D*) the extreme upper range of pressure with hypertension and an xtreme lower range f press re with hypotension; the diastolic pressure in aortic regurgitation may drop almost to 0 (broken lines) (*E*) the variability of the systolic pressure (from 250 to 200) nd of the diastolic pressure (from 150 to 125) possible over an interval of 10 minutes in given case of hyperpiesis,

normally low systolic blood pressure are vasomotor or vascular shock. Addison's disease, and, to a lesser degree, acute and chronic constrictive pericarditis, and aortic stenosis.

The *diastolic* arterial blood pressure range is normally much less than the systolic; a low reading in an adult is 60 mm of mercury and a high 90 It records the basic pressure in the circulatory system and so is fundamentally more important than the systolic pressure which is but very transient at its full height.

The causes of abnormal increase of the diastolic blood pressure are the same as those recorded above for the systolic pressure. The causes of abnormal decrease of the diastolic pressure are the same as for decrease of systolic pressure, and, in addition, aortic regurgitation.

In late years, particularly in France, much interest has been expressed in the so-called *average dynamic* or *mean effective* blood pressure which is the total pressure leveled off from the peaks and hollows of systolic and diastolic pressures, that is, such a pressure as would assure during a certain interval of time a steady flow of the same amount of blood as passes through a given vessel under the variations of pressure ordinarily found with each heart cycle. This mean effective or average dynamic blood pressure gives, to be sure, a better idea than any other reading of the total pressure strain on the circulation, but it has the defects of not taking into account the swing of the pulse pressure, which is important, and of being difficult to estimate accurately. Although Vaquez and his associates (1932 and 1933) thought that the maximal oscillation of the pulse excursion just above the diastolic level in sphygmomanometry represents with sufficient accuracy the mean pressure. Moreover the "mean pressure" is usually close to and parallel with the diastolic blood pressure, the level of which may be used as an adequate guide, along with the pulse pressure. Wiggers (1942) called attention again to the mean pressure but emphasized rather the importance of the pulse pressure.

The *pulse pressure* is the difference between the systolic and diastolic pressures, normally ranging in an adult at rest from 40 mm (for example, with systolic pressure of 120 and diastolic of 80) to 70 (for example, with systolic pressure of 140 and diastolic of 70)

An abnormal increase of pulse pressure is most commonly due either to an especially high systolic pressure in systemic hypertension (pulse pressure of 120 mm, for example, with systolic pressure of 220 and diastolic of 100) or to a low diastolic pressure in aortic regurgitation or marked peripheral vasodilatation (pulse pressure of 110 mm, for example, with systolic pressure of 140 and diastolic of 30) An abnormal decrease of pulse pressure is most commonly found in states of vasomotor shock with or without syncope (15 mm, for example, with systolic pressure of 65 and diastolic of 50) aortic steno-

and (F) auscultatory gap averaged in series of 30 cases showing this phenomenon (26 with hyperpiesia, 2 with hyperpiesia and aortic stenosis, and 2 cases f aortic stenosis without hypertension. 205 mm = average systolic pressure, 97 mm = verage diastolic pressure, and = verage auscultatory gap, ranging from 177 to 150 mm)

sis (25 mm, for example, with systolic pressure of 110 and diastolic of 85), acute or chronic constrictive pericarditis (20 mm for example, with systolic pressure of 105 and diastolic of 85) or adrenal insufficiency in Addison's disease (20 mm, for example, with systolic pressure of 80 and diastolic of 60).

A very abnormal and clinically significant variation of pulse pressure is an alternation found when the heart rhythm is regular or after premature beats (extrasystoles) and due chiefly to a fall in systolic pressure of a few millimeters (2 or 3 to 20) every other beat, this is the *pulsus alternans* a sign of serious weakness, and probably of alternating strength of contraction, of the left ventricle when the pulse is not excessively fast (see Chapters 8 and 30)

The blood pressure in children is less than in adults, beginning at about 65 systolic and 40 diastolic in earliest infancy and rising slowly to the adult levels soon after adolescence.

Finally it is important to note that the usual blood pressure readings refer to the pressure in the brachial artery on one side. It is often wise to measure the blood pressure in both arms (especially if there is suspicion of syphilitic aortitis) and to repeat blood pressure measurements several times at intervals of a few minutes if abnormal readings are found at first. The pressure in other arteries of the body varies according to their size, position, and state of contraction. Thus, the blood pressure in the aorta is normally greater than that in the brachial artery while that in a digital artery is considerably less. The pressure in the femoral artery is greater than that in the brachial artery for four reasons (1) its larger size (2) the greater bulk of soft tissue mass to be compressed in the leg, (3) the lower position of the femoral artery in the body in the upright position, hydrostatic pressure thus adding its effect, and (4) a certain amount of compensatory vasoconstriction in the lower part of the body in the erect posture. Localized vasoconstriction may occur still further to vary the pressures, and sometimes exposure of a part of the body (the arm for example) to cold causes a general vasoconstriction, excessive in hypertensive cases and perhaps in potential hypertensive cases (see Chapter 31) Hardness of the arterial wall affects little or not at all the blood pressure readings made by the various indirect methods (Dameshek and Loman, 1932 Ayman and Krakower 1933) although loss of elasticity of the walls of the larger arteries favors a larger pulse pressure. The act of compression of the arm may itself reflexly affect the first blood pressure levels, and not simply from apprehension, so that several readings are sometimes necessary I find that it is best for this very reason to inflate the cuff at first only a little above the diastolic pressure and to record that reading during decompression before inflating to a much higher pressure to obtain the systolic reading, especially in hypertensive patients.

Pulmonary arterial blood pressure. During the past few years one of the most desired and needed advances in human physiology has come to pass, namely the measuring and recording of the blood pressure in the pulmonary circulation by means of cardiac catheterization and electrical or optical manometer (Dexter et al 1947) (see Figure 18) In fetal life the pulmonary

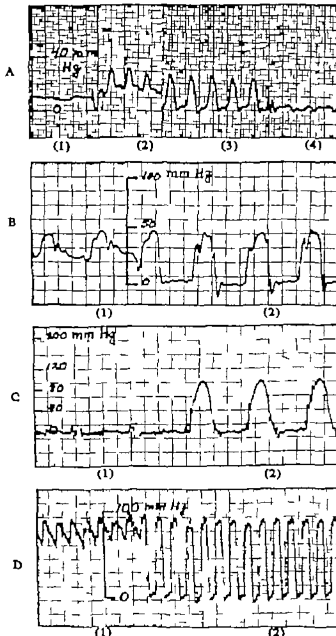


FIG. 18 Blood pressure by cardiac catheterization. (Kindness of Dr Gordon S. Myers, Massachusetts General Hospital, Boston.)

A. In a normal 36-year-old man
1. Standardization in millimeters of mercury
2. Pulmonary artery pressure
3. Right ventricular pressure
4. Right atrial pressure

B. In a 24-year-old woman with mitral stenosis
1. Pulmonary artery pressure
2. Right ventricular pressure

C. In a 19-year-old female with pure pulmonary stenosis of high degree
1. Pulmonary artery pressure—abnormally low with feeble pulsations
2. Right ventricular pressure—very high

D. In 3-year-old girl with tetralogy of Fallot
1. Tip of catheter overriding aorta
2. Pressure in right ventricle

circulation is minimal, but the right ventricle maintains through the patent ductus arteriosus the major part of the systemic circulation and is larger than the left ventricle. Soon after birth when the ductus arteriosus closes, the pressures of pulmonary and systemic circuits are undoubtedly very nearly equal hence, at birth it may be said that the pulmonary blood pressure probably measures about 50 to 60 mm of mercury since that is the systemic blood pressure at this time. Normally the right ventricle fails after birth to maintain the systemic circulation and, therefore, the pulmonary blood pressure quickly falls below the level of the systemic pressure, since the short, rapidly dividing, pulmonary arterial tree produces relatively little resistance. In the human adult the systolic blood pressure in the main pulmonary artery measures normally 15 to 35 mm of mercury with average of 25 mm (Figure 11) and the diastolic pressure is about 10 mm of mercury On the other hand when the pulmonary circulatory resistance is much increased as in high-grade mitral stenosis, left ventricular failure, pulmonary endarteritis, or severe chronic pulmonary disease, the pulmonary arterial pressure rises considerably and may even surpass the systemic arterial pressure, as further indicated by the fact that in some cases the right ventricle actually exceeds the left ventricle in size and weight. A rough check on the relationship between, but not the actual levels of the systemic and pulmonary arterial pressures can be made by comparing the intensities of the aortic and pulmonary second heart sounds.

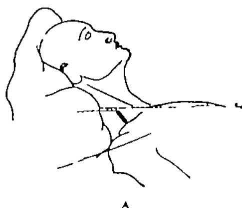
Periodic variations of pulmonary blood pressure of considerable extent have been found to occur in experimental animals and also in man with respiration. Both systolic and diastolic pressures fall with inspiration and rise with expiration, the systolic more than the diastolic. Also during cycles of apnea and hyperpnea the pulmonary blood pressure varies, the systolic pressure falling and the diastolic rising during apnea.

Intracardiac blood pressure. It has become possible since the publication of the third edition of this book to measure accurately and to record in man the blood pressures in the right heart chambers by intracardiac catheterization (Cournand, et al., 1944) and the use of a manometer (Hamilton) or a more recently devised electromanometer (Figure 18) Normally in the human adult the right atrial pressure under as basal conditions as can be attained measures from +2 or +3 to −2 or −3 mm of mercury averaging 0 mm and the right ventricular pressure ranges from +15 to +35 systolic and from 0 to +2 mm diastolic. The pressure in the left heart chambers is, as yet, not determinable normally but the left atrial pressure has been measured directly in the case of a congenital atrial septal defect, being about +5 to +10 mm of mercury therewith, and at operation in mitral stenosis, being found to measure about +30 mm, varying with the degree of valvular obstruction.

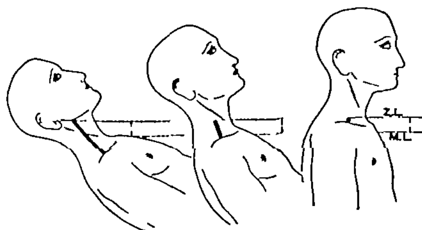
Venous blood pressure. The venous blood pressure was measured two hundred years ago by Hales, who inserted a manometer directly into the jugular vein of a mare (Hales, 1733)—see quotation at the beginning of this chapter The venous blood pressure may be measured with a fair degree of accuracy as has been shown by ascertaining the actual pressure level vertically above

the level of the junction of the superior vena cava and the right atrium (approximately one third the distance through the chest from front to back at the lower border of the third right sternocostochondral junction) to which blood will rise or displace normal salt solution in a tube connected by trocar or needle with an arm vein (Moritz and von Tabora, 1910; Holt, 1940) or more conveniently by a spring phlebomanometer connected with the vein (Burch and Winsor 1943) In logical evolution from these cruder technics the newest and most accurate, though not exactly routine, method of venous blood pressure measurement is by intravenous catheter and special electromanometer

A simple, but generally adequate, clinical method of determining the



A



B

FIG. 19 The level of the height of the blood column in the jugular vein. (*A*) In a normal person, recumbent. (*B*) In person with increased systemic venous pressure, in different inclinations of the body Z.L. = zero level; M.L. = manubrial line. (Lewis, T *Diseases of the Heart* 4th ed. The Macmillan Company New York, 1946.)

venous pressure, requiring no apparatus except a centimeter scale, is to measure the height above the lower border of the third costal cartilage at the right border of the sternum (level of mouth of the superior vena cava) to which the blood rises in the jugular vein with the subject sitting upright; if the pressure is within the normal range, that is, below 10 cm the vein will not be evident, and if it is very high, that is, above 25 cm, the blood column will rise out of sight under the ear: slight to moderate elevations can be readily measured (Figure 19) A third but now outmoded method is by determining the amount of air pressure (best measured in centimeters of water) necessary to collapse a superficial vein of moderate size in forearm or hand. An apparatus for making such a measurement has already been mentioned (page 110) Obesity thick skin, or sclerosis of the veins may make such determination difficult.

The normal venous pressure varies widely from 4 to 10 cm of water (about 1½ to 6 mm of mercury) Usually it amounts to about 6 to 7 cm of water being about one half in millimeters of water of the normal arterial pressure in millimeters of mercury and therefore about 1/20 of the arterial pressure The systemic blood pressure thus drops from, say 130 to 5 mm of mercury as it progresses from brachial artery through its branches, and through arterioles, capillaries, and venules, to a superficial vein of moderate size on the back of the hand or on the forearm. If the venous pressure by the usual method measures 10 cm or more of water it is abnormally high. Exercise may temporarily raise the pressure considerably even as high as 20 cm of water but the three conditions which are associated with abnormally high venous pressure at rest, even to 30 cm of water or more, are congestive heart failure of considerable or moderate degree, acute or chronic constrictive pericarditis, and venous obstruction due to thrombosis or compression. If the right ventricle remains competent while the left ventricle has failed, there is pulmonary congestion and increased pulmonary venous pressure due to left ventricular weakness, even though the systemic venous pressure remains normal.

A very interesting phenomenon is encountered in some cases with well-marked tricuspid regurgitation without much constant distention of the systemic veins, consisting of a considerable *systolic jugular pulse* most pronounced in the deep veins in the neck. In such cases the venous pulse pressure, which is usually very small or nonexistent, may be marked, up to 50 or 60 mm, and so striking that the jugular pulse may be wrongly interpreted as the carotid pulse (White and Cooke, 1939)

Another interesting phenomenon consists of the *paradoxical inspiratory filling of the jugular veins* due to the inability of the right heart chambers, either because of constrictive pericarditis or severe right heart failure, or of an obstructed superior vena cava, to pass on the extra blood they receive from the systemic veins as the result of the increased negative intrathoracic pressure during inspiration (Hitzig, 1942)

In general the venous pressure determination is not of great clinical value inspection of the veins to determine their degree of engorgement usually sufficing without exact measurements. It has been suggested, however that a

figure of 20 cm of water of venous pressure in heart failure is a useful indication of the therapeutic need and value of venesection.

We can now measure the blood pressure in the great veins in man by catheter and special manometer. It varies normally in the human adult from +3 to +5 mm of mercury with great increase when the heart fails or in chronic constrictive pericarditis. In the experimental animal the blood pressure in the great veins has been found to be much lower than that of the smaller veins, dropping almost to zero in the venae cavae. This is to be expected with the slowing of the blood stream resulting from the merging of many venous channels into the narrow limits of a few for even though these few are of large caliber their total capacity is far less than that of the peripheral veins. Fortunately to aid in the return of blood to the heart there are four factors, the most important of which is the intrathoracic negative pressure. The effect of intrathoracic suction during inspiration is marked and in the experimental animal may more than quadruple the actual venous pressure in the great veins to establish the effective venous pressure. For example, in the dog a venous pressure of 10 mm (1 cm) of water may be increased through the action of this negative intrathoracic pressure to an effective pressure of 50 mm of water in the right atrium. Poor action of the diaphragm and disturbances of respiration limiting the negative intrathoracic pressure and especially obstruction to the venous return flow to the heart through congestive heart failure, chronic constrictive pericarditis, pericardial effusions, or mediastinal tumors or adhesions, affect very easily and obviously the venous blood return to the heart on account of the low pressure that is usual in the great veins. This is particularly true of the portal system where the blood has to flow through two sets of capillaries and enter the inferior vena cava by way of the hepatic veins which empty at a considerable angle into the vena cava.

The three other factors aiding the return of venous blood to the heart are the tonus and movement of muscles which compress the veins, the valves in the veins which help to keep the blood going in the right direction, and on occasion, as needed, arteriolar and capillary dilatation to allow a speeding up of the blood flow into the veins and thence to the heart.

For a discussion of capillary blood pressure see Chapter 8 under Capillary Circulation.

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CHAPTER 7

CARDIOVASCULAR ROENTGENOLOGY

In the present edition this chapter has been profitably shortened, several helpful new illustrations have been added, and a number of pertinent references to the literature published since 1943 have been appended to the Bibliography

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"During the past two or three months I have been much interested in studying the X-rays, and with the assistance of Mr C. L. Norton and Mr R. R. Lawrence, of the Massachusetts Institute of Technonogy who have been investigating the X-ray problem in the Rogers Laboratory of Physics, have tested the application of X-rays to medicine in various ways. Their application to surgery was soon evident;

"But I wish especially to direct your attention to some of the medical rather than the surgical uses of these magical rays, and especially to their use with the fluoroscope' in the fluoroscope with a screen of tungstate of calcium the parts of the body which are most easily passed by the X-rays appear lightest on the screen, those which are densest being darker The lungs are easily penetrated,

"The pulsations of the heart may be followed with the fluoroscope, not only the ventricular but also the auricular contractions and dilatations.

"In the following cases the usual physical examination and that made with the fluoroscope corresponded very well

"Case I —*The first medical case I examined was that of a* man with an enlarged heart (seven inches in transverse diameter) I found that the outline of the heart, as seen from the front of the body through the fluoroscope, corresponded in a general way to the outline drawn on the skin with percussion as a guide. It was interesting to note that the heart could be made out through the man s waistcoat and two shirts.

INTRODUCTION

Cardiovascular roentgenology (*Röntgen*, 1895 and λόγος, knowledge) or radiology (*radius* ray and λόγος, knowledge) has become firmly entrenched as an important part of routine study of the heart and blood vessels' it ranks

fourth in value as a method of examination after history taking, physical examination, and electrocardiography Although in cardiovascular diagnosis the roentgen ray usually supplies but confirmatory evidence sometimes surprising and frequently useful and interesting information results from such routine study Only by this method may the size and shape of the heart be determined with certainty during life, the size and shape of the left atrium, aorta, and lung hiluses be ascertained at all, and calcification in pericardium, heart muscle valves, or deep blood vessels be actually visualized. On the other hand,

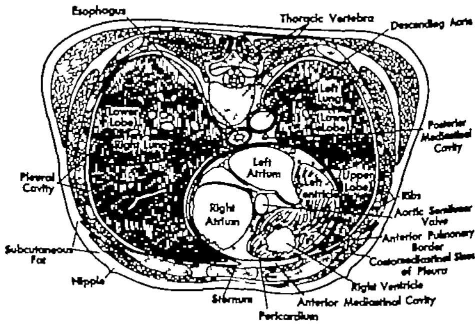


FIG. 70. Anatomic drawing showing cross (horizontal) section of thorax and heart at level of the eighth thoracic vertebra. (Sobotta and McMurrich, *Atlas and Textbook of Human Anatomy* 1906. Kindness of W B Saunders Company Philadelphia)

it must be admitted that serious heart disease may be present, as discovered in other ways, when no clue is given to its presence by roentgenology Also early and slight cardiovascular lesions usually escape notice in the roentgen ray film because the heart and vessels may show no definite abnormalities of size shape, or action. For the most part, therefore, roentgenology merely reveals evidence of well-established or advanced disease which is difficult or impossible to eradicate. Yet it does help the practitioner of medicine appreciably in the establishment of exact diagnosis which are so essential to accuracy of prognosis and to the handling of patients with chronic heart disease.

The chief difficulty in the routine application of roentgenology to the circulation lies not in the technic which can be mastered without great difficulty but in the interpretation of the normal limits of heart size, shape, and action, and therefore in the diagnosis of slight abnormalities. There are so many factors, for example, age, size, build, respiration, and nervousness resulting in in-

dividual variations within the normal (see Figures 2 3 and 6 in Chapter 2) that it is at present impossible to recognize them all, or at least to take them all into consideration in the establishment of any satisfactory tables of measurement of size, or rules about shape or action. Not only are the normal limits difficult or impossible to define accurately but in a given individual important changes may occur in heart size or shape, insufficient to produce definite roentgenologic abnormalities at the time of examination, which would be noted if comparative studies had been previously made. For example, a heart showing in an anteroposterior teleroentgenogram a shadow area of 80 sq cm at the lower limit of the normal figures may increase in area 38 per cent before it equals even the average normal measurement (110 sq cm) and as much as 75 per cent before it equals the upper normal limit of 140 sq cm in the case of a person with a body surface area of 1 8 sq meters (Smith and Bloedorn, 1922) Successive records of heart size and shape in the same individual carefully made under varying conditions of health should be more useful than a single comparison of this individual case with a table of normal averages or a set of rules It is, however often impossible to possess information about the roentgen ray findings prior to the onset of trouble in a given case. In spite of these difficulties some rules are necessary and normal standards for measurements of size are useful if we realize their inaccuracy in application to individual patients and do not lull ourselves into a false sense of security which tends to develop from the use of figures and formulas.

METHODS OF CARDIOVASCULAR ROENTGENOLOGY

Roentgenology of the heart includes seven procedures, the first three of which are commonly used, and the last four in special cases or for some particular study They are as follows (1) fluoroscopic examination, (2) orthodiagraphy (3) teleroentgenography (teleradiography) (4) (roentgen) kymography (5) (roentgen) tomography (planigraphy) (6) visualization of heart chambers and greater and lesser arteries and veins by the injection of radio-opaque media (e.g. Diodrast) into the blood stream, and (7) roentgencinematography At the present time the first method is used universally by the most careful workers everywhere, but the other methods are rarely used together There is a division into two schools, that employing orthodiagraphy and that using teleroentgenography Each of these methods has certain advantages which will be presented below but in each case fluoroscopy should be, and ordinarily is, employed along with either orthodiagraphy or teleroentgenography The seven procedures mentioned above will be briefly summarized herewith.

1. Fluoroscopy (φλύειν to flow out, ῥοῦς, current, and σκοπεῖν to examine) Fluoroscopic examination consists in the study on the fluorescent screen of the projection of the heart shadow in its various parts and in toto, and with the thorax of the subject in various positions in contact with the screen. If possible the subject should, in harmony with several other methods of ex

amination—inspection, percussion, and auscultation—be examined chiefly in the upright position. Although the tube may be placed at a distance (2 meters or more) from the thorax for the purpose of seeing the heart and great vessels relatively undistorted by divergence of rays (telefluoroscopy) as in the case of teleroentgenography this is not essential, inasmuch as accurate measurements can be obtained by orthodiagraphy nor is it practicable, since so much extra energy is required (about 16 times as much as is needed with the tube at 50 cm) In fact the very magnification of the details and activity of the heart shadow by the divergent rays is helpful, and one quickly becomes accustomed to the degree of distortion. Also, the illumination is better with the tube nearer than at a distance, especially in the oblique or lateral views.

The first position studied is most conveniently the *anteroposterior*[1] with the patient erect, facing the observer squarely and leaning his anterior chest wall against the screen with the tube behind him After all parts of the heart and great vessel shadows have been carefully examined in this position, the contour and action of the whole heart observed, the action of the diaphragm noted along with the effect of deep inspiration and expiration, and the lung shadows and especially the hiluses studied, the patient should then be rotated slightly to the left so that the right anterior side of the chest wall touches the screen. This is called the *right anterior* or *first oblique position*. To improve the view in this position, the right hand should be held behind the head and the left hand on the left hip with the elbow forward. Still further rotation in the same direction, to the *right lateral* and *right posterior oblique positions*, may then be carried out if desired, but this is usually not necessary study in the right anterior oblique position sufficing. In a similar way the patient is rotated to the right from the anteroposterior position until the left anterior part of the chest wall touches the screen. This is called the *left anterior* or *second oblique position*. The left hand should be held behind the head and the right hand on the right hip Again further rotation in the same direction may be carried out if desired, to the *left lateral* and *left posterior oblique positions*. And finally the patient may be examined with his back squarely against the fluoroscopic screen, in the *posteroanterior position* to emphasize abnormalities of the descending thoracic aorta, but this position is rarely of any value. For routine fluoroscopic examination the three positions, anteroposterior right anterior oblique, and left anterior oblique ordinarily suffice. An important part of the whole examination includes careful observation of heart and vessel shadows during the process of rotation from one position to another this may explain certain abnormalities, the cause of which is not obvious in the positions themselves. Fluoroscopic tracings, not orthodiagraphic, are sometimes

[1] Throughout the book the position of the subject in roentgenologic examination is designated according to the axis termination at the screen or film, as has been customary and not at the tube: thus "anteroposterior" signifies that the front of the chest rests against the screen, "right anterior oblique" means that the right anterior chest wall is against the screen, and so on. If the designation "posteroanterior" is employed in the place of the customary "anteroposterior" "left posterior oblique" must be similarly employed instead of "right anterior oblique" to be consistent, but this change is neither necessary nor convenient.

made in one or more positions to study outline shapes, but these are of limited value.

2. Orthodiagraphy (ὀρθός, straight, διά, through, and γράφειν to write) (Moritz, 1902) An orthodiagram is a tracing, made by the observer of the shadow of the heart and great vessels outlined against the fluoroscopic screen by the *central rays* from the roentgen tube Its advantages are that it is very accurate if well done, because the rays used are exactly parallel, that observation of the heart in action allows accurate determination of the position of the apex and of junctions of atria and ventricles or of great vessels and heart, which may not be possible in any other way that it requires fluoroscopic observation, not always carried out with teleroentgenography and, finally that it is an inexpensive method of obtaining permanent records of the shadow of the heart and great vessels It has the disadvantages of incompleteness of total detailed *picture of heart and thorax, and of easy possibility of subjective* errors in untrained or careless hands.

3. Teleroentgenography (τῆλε, far away *Röntgen*, the discoverer and γράφειν to write) or teleradiography (Köhler 1905) The other method in routine use for obtaining a graphic record of the heart shadow by roentgen ray from which a fairly accurate idea of heart size and shape can be obtained is teleroentgenography (teleradiography) A teleroentgenogram is a record on film or plate of the shadow in whole or in part, of the heart and great vessels cast by the roentgen rays with the tube far enough away (2 meters or 6 to 7 ft) from the chest and plate for reasonable accuracy At 6 to 7 ft the error of heart size measurement is, however still appreciable, the excess in transverse cardiac diameter *in the normal adult being from 1 0 to 1.5 cm (8 to 12 per* cent) and as great sometimes in pathologic cases as 2.5 cm the excess is still more evident in the measurement of surface area. Certain factors enter in as variables to increase or to decrease this error They are chiefly heart size and thickness of the anterior chest wall. The larger the heart, the greater is the error because the rays outlining its shadow are more divergent than are those outlining the shadow of a small heart. Even the ratio of heart size to thorax size ("the cardiothoracic ratio) differs in the two technics, being slightly less in teleroentgenography than in orthodiagraphy because the maximal frontal plane of the heart lies anteriorly to that of the thorax (see Figure 20 page 126) The advantages of the teleroentgenogram are as follows (1) it is a more objective record than an orthodiagram, and so less liable to subjective sources of error provided the technic be accurate (2) it is a more complete record than the orthodiagram giving greater detail, and demonstrating clearly differences in position of the thorax, which differences may render inaccurate comparative measurements of heart size at different times (3) it outlines more clearly hazy or otherwise indefinite borders (4) it can be satisfactorily carried out by a *well-trained and careful technician, the actual measurements and in*terpretation being made from the finished film by the physician.

4. Kymography (κῦμα, wave, and γράφειν to write) About twenty years ago there was introduced (Stumpff, 1931) an ingenious application of roent

genography to the study of the degree and direction of pulsation of the heart and great vessels, first suggested by Sabat (1913) By the use of a grid of lead strips with narrow slits between them it is possible to record the systolic and diastolic heart and vessel borders of limited alternating sections of the heart shadow when the film moves at a uniform rate across the slits at a speed which allows several pulsations to be recorded for each of the shadow sections. The grid may be placed vertically diagonally or radially and the screen or the grid may move in any direction, but the usual and most practicable and instructive arrangement is for the grid to be fixed in place with the slits *horizontal* and for the film to descend vertically In the resulting kymogram (see Figure 21) the innermost limits (valleys) of the excursions normally represent systole in the case of the heart shadow and diastole in that of the shadows of the great vessels, while the outermost limits (peaks) normally represent diastole in the case of the heart shadow and systole in that of the shadows of the great vessels. In certain disease conditions there are distortions of these pulsations, an increase, for example, in cases of aortic regurgitation so far as left ventricle and aorta are concerned, or of the whole heart and both aorta and pulmonary artery in thyrotoxicosis, a decrease in cases of great myocardial weakness, myxedema, or constricting pericardium, or an absence or even a reversal of the pulsation (called paradoxical) of a limited portion of the left heart shadow border at, or more often just above, the apex in the case of a moderately large cardiac aneurysm or myocardial infarct. There is not a great deal of clinical value in roentgenkymography except in occasional confirmation or discovery of a myocardial infarct from coronary occlusion, the differentiation at times of aortic aneurysms from other types of mediastinal tumors, the separation of the shadows of atria and ventricles, and in the course of complete study of rare or puzzling cases.

An interesting new method of recording the action of the heart fluoroscopically has been introduced through Chamberlain by Henny and Boone (1945) by the use of the photoelectric cell placed over any desired portion of the heart border and connected with galvanometer Simultaneous tracings can be made of the electrocardiogram or of carotid pulse or heartbeat itself also recorded electrically Figure 22 shows examples of normal and abnormal curves, which have been variously called *electrokymograms* or *electrofluorograms*. Not only may records be made of the pulsation of atrial and ventricular borders and of that of the great vessels, superior vena cava, aorta, pulmonary artery and its branches in the lung hiluses, but so-called *densograms* can also be made over the main heart shadow itself and over the lungs, presenting curves of the variations in the thickness of the underlying mass. These electrokymograms present a clearer and simpler record of the cardiovascular motions than the films that have been customarily taken in the past (Figure 21) and will probably supersede them. They have the same function, however in revealing or confirming such diagnoses as myocardial infarction of significant extent and of certain aneurysmal dilatations of the great vessels. Also they have been used in an effort to measure the stroke volume of the heart.

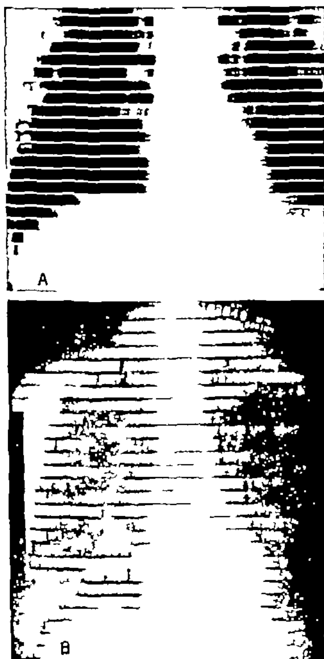


FIG 21 Kymograms (roentgenograms) of thoraces of (*A*) normal individual (kindness of Dr Richard Schatzki, Mt. Auburn Hospital, Cambridge, Mass.) (*B*) case with myocardial infarct (kindness of Dr George Levene, Massachusetts Memorial Hospital, Boston)

5 **Roentgentomography** (*Roentgen*, *τόμος* a cut or section, and *γράφω* t write) or laminagraphy (Latin *lamina* layer and *γράφειν*) or planigraph (Latin, *planus* a level, and *γράφειν*) There has also been introduced in rece years a method of x-ray study of the thorax that is helpful particularly i locating in three dimensions the exact position of lesions in the lungs. It i of much less importance so far as the heart is concerned but the method ha not in that direction been wholly explored as yet. Tomography consists in th

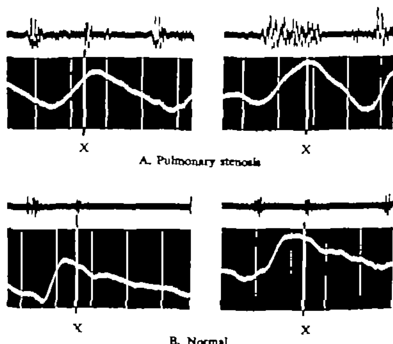


FIG. 22. Electrokymograms and simultaneous phonocardiograms taken at the pul monary valve area of (*A*) two patients with pulmonary stenosis and (*B*) tw normal individuals. Not the slow upstroke in the electrokymogram of the two patients wi pulmonary stenosis. Time = 0.04 and 0.20 second, X = time of second heart sound (Kindness of Mr M. A. Rappaport, Sanborn Company Cambridge.)

recording of body shadows at varying depths by exact focusing of the x-rays —thus the anterior and posterior regions of the thorax may be blurred while a sharp outline is obtained of a *vertical frontal plane in midthorax*. It is possible by this means to obtain clearer pictures of the atria and pulmonary vessels or of the aortic arch or descending aorta.

6. **Radio-opaque visualization.** In obscure or special cases the injection of a radio-opaque medium, most commonly Diodrast, into veins or arteries of arms or legs and very recently even directly into the ventricles themselves (Ponsdomenech and Nuñez, 1951) has proved helpful in establishing a detailed diagnosis of abnormalities of blood vessels or heart chambers that might be impossible in any other way (Figures 23 24 and 148 page 779) Considerable experience in both injection and roentgenographic technic is neces-



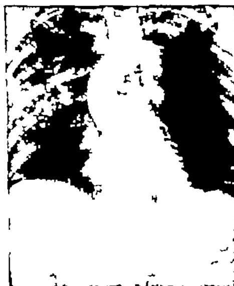
A B C

FIG. 23 Roentgen films of chest of male, ge 40, with shadow in region of aortic arch. (*A*) Anteroposterior view (*B*) Left anterior oblique view immediately after Diodrast injection showing filling of right ventricle and pulmonary arterial tree. (*C*) Film few seconds later showing filling of the left ventricle and aorta. This method of technic of Diodrast injection establishes at once the diagnosis of mediastinal tumor versus aortic aneurysm. (Kindness of Dr B J W lsh, Washington, D C.)





A





B

FIG. 4 (*A*) Diodrast -ray pictures showing the filled right ventricle and pulmonary artery in the anteroposterior and left anterio oblique views in the case of normal heart. (*B*) Diodrast -ray pictures showing the filled left ventricle in the case of a normal heart with diseased right l ng. (Kindness of D E. R. Poondomenech and Dr V B Nuñez, H ana, Cuba.)

ary to obtain the best results, but the method should be made available in every teaching hospital and is helpful in differential diagnosis, especially in congenital heart disease.

7 **Roentgencinematography** Finally a seventh method of roentgen ray study of the heart, of interest from the standpoint of special investigation or teaching, is that of cinematography The most practicable way which has recently been developed, consists of cinematography of the shadow as it is seen on the fluoroscopic screen (Reynolds, R. J., 1934 Janker R., 1936 Rushmer 1949)

THE SHAPE, SIZE, AND ACTIVITY OF NORMAL HEART AND GREAT VESSELS STUDIED BY ROENTGEN RAY

The shape of the normal roentgen ray heart shadow is quite variable being dependent on a number of factors. The heart shadow should be outlined during quiet respiration and preferably in the sitting position, for forced respiration causes abnormalities of shape and size, and the standing and recumbent positions may appreciably affect the heart. Marked changes have been experimentally produced by certain respiratory efforts, the heart shadow increasing considerably in size with the Müller experiment (an attempt to inspire forcefully with the glottis closed) and decreasing considerably in size, sometimes to appear like the cor pendulosum (pendulum heart) with the Valsalva experiment (an attempt to expire forcefully with the glottis closed) a fact of considerable interest (Crowden and Harris, 1929) such experiments produce, however, very artificial conditions, not comparable to clinical findings. The decrease in heart size during the Valsalva experiment is due to the prevention of entrance of blood into the heart by the increased intrathoracic pressure, while the increase in heart size during the Müller experiment is due to the increased flow of blood into the heart resulting from the markedly negative intrathoracic pressure. So far as position of the subject is concerned, the heart size and therefore its shadow may be considerably decreased in the standing position (due to much decrease in the return of blood to the heart in that posture) while there may be a considerably increased return of blood to the heart and increased content of blood in the lung vessels in the recumbent position resulting in a physiologic dilatation (Zdansky 1936) In reporting or recording roentgen views of the heart a statement should always be made as to the position of the patient, and also the phase or state of respiration. To study the heart (in contrast to the lungs) it is best to make the examination and the films during very quiet respiration, which is essentially midway between full inspiration and full expiration. There can be great distortion of the heart shadow with marked decrease in size if the films are taken while the breath is held in full inspiration, a common practice in study of the lungs (Figure 3C, page 32) For further observations concerning the range of the normal heart the reader is referred to Chapter 2.

Anteroposterior view In the anteroposterior view the shadow of heart and

great vessels is roughly egg shaped with apex diagonally down and to the subject's left and with the great vessels attached as a pedicle at the left side of the base (Figure 25) If the diaphragm is high the heart lies more horizontally and to the left, and there is a more acute angle between it and the great vessels (Figure 3 page 32) If the diaphragm is low the heart lies more vertically and centrally in the body seems narrower (because of this change of position and of the resultant rotation to the left) and hangs down from the great vessels with much flattened angle (Figure 3)

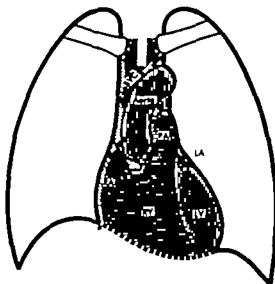


FIG. 25 Drawing of normal x-ray heart shadow with the various chambers and great vessels indicated. (Kindness of Sir John Parkinson and the *Lancet* London.)

SVC, superior vena cava — RV right ventricle
PA, pulmonary artery — LA, left atrium
RA, right atrium — LV left ventricle

The borders of the anteroposterior shadow of the heart and great vessels are three in number because of the roughly triangular shape they are right, left, and inferior Unless concealed by abnormal shadows in lungs, pleurae, pericardium or mediastinum the right and left borders are easily seen. The inferior border is seen with difficulty or not at all concealed as it is by intra-abdominal shadows, unless there is sufficient air in stomach or intestines to make its outline visible. Its whole extent is seen in only two conditions (1) pneumoperitoneum and (2) interpolation of colon between heart and liver The upper border of the heart at the junction of the great vessels is not seen except at its outer ends

1 *The right border* (that to the right of the sternum of the subject, not on the observer's right) is composed of three parts. The uppermost is a rather faint, straight, vertical edge extending slightly outward and to the right from below up and not always clear It is produced by the shadow of the

right border of the superior vena cava and innominate vein, at the upper part overlying the innominate artery the artery itself if dilated or prominent, may form the shadow edge. The second part (next in order below) is the straight edge of the superior vena cava or more commonly the slightly convex shadow of the right edge of the ascending aorta superimposed on the superior vena cava shadow and making up a second quarter or more of the whole right border the inwardly directed curve of this aortic shadow to the left can often be made out overlying the fainter shadow of the vena cava. The third part of the right border of the heart shadow is the moderately convex shadow of the right edge of the right atrium from a point just below the mouth of the superior vena cava down to the inferior vena cava, which can in rare instances be barely seen as a very short straight line quickly disappearing into the shadow of the diaphragm, this right atrial shadow makes up the lower third to half of the right border of the shadow of the heart and great vessels.

2. *The left border* of the shadow of the heart and great vessels is considerably longer than the right (about 50 per cent longer) and is made up normally of four parts. The uppermost part is a short convex curve close to the apex of the whole shadow and is directed up toward the left shoulder of the subject it is variable in prominence and is due to the shadow of the upper and left edges of the aortic arch and beginning of the descending aorta. The second part is a slightly convex curve just below usually slightly longer than the first but making a considerable angle with it, directed downward from the subject's right to his left, and often almost continuous in direction with the left border of the main shadow of the heart itself which lies below the trunk of the pulmonary artery and its left main branch cause this convexity Third, and next below for a very short distance and forming a straight or slightly convex line lies the left border of the left atrial appendage, often not distinguishable from the edge below it unless its presystolic pulsation happens to be seen or there is marked left atrial bulging. And, fourth, the major part, two thirds to three fifths, of the left heart and great vessel shadow border is caused normally by the left ventricular shadow forming a slightly or moderately convex line, sloping to the subject's left from above downward, and becoming more definitely curved downward as the apex is approached.

3 When *the lower border* of the heart shadow is visible it is made up of the apex and lower border of the left ventricle on the extreme left; then for one half to three quarters of the distance to the subject's right heart border it is caused by the right ventricular shadow and for the rest of the distance, to the right of the midsternum, by the right atrium. However varying positions of the heart alter these relations for example, in the case of the drop or vertical heart little or none of the right atrium forms the lower border of the heart shadow When this lower border is visible it is slightly convex near the apex but fairly straight from there on.

The peak of the heart and great vessel shadow is blunt and obscure except where the aortic arch is visible on the subject's left, but in some cases the aorta, crossing above the pulmonary artery to form the arch, can be seen. This

peak of the great vessel shadow is more cylindric than cone-shaped, being an elongated pedicle.

Right anterior oblique view In the right anterior or first oblique view (Figure 26) the shadow of the heart and great vessels shows in front from below upward the convex curve of the right ventricle if the subject is sufficiently turned if the rotation is slight the left ventricle may be seen. At the upper third of this anterior edge the pulmonary artery and aortic shadows appear and the latter sweeping over in a long curve loses itself in the shadow

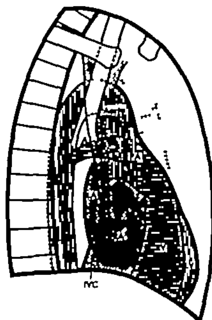


FIG. 26. Drawing of shadows of normal heart and great vessels in right anterior oblique position with various chambers and great vessels indicated. (Kindness of Sir John Parkinson and the *Lancet* London.)

IVC, inferior vena cava	RA, right atrium
PA, pulmonary artery	RV right ventricle
LA, left atrium	LV left ventricle

of the spine posteriorly Under this aortic shadow and at the upper part of the posterior border of the heart shadow lie the bifurcations of the trachea and of the pulmonary artery Below this are the straight or slightly convex borders of the two atria, the left above the right and the latter extending down to the diaphragmatic shadow where the inferior vena cava may be just visible. The anterior and posterior mediastinal spaces should be clear and the trachea and bronchi are usually to be seen. The left ventricle is concealed at the back of the heart shadow in this position (note Figure 20)

Left anterior oblique view In the left anterior oblique view (Figure 27) the heart is seen, as it were, almost in sagittal section both ventricles and both atria being evident, the two former making up the lower two thirds of the

heart shadow the right in front and the left in back, and the two latter making up the upper third of the shadow the right in front and the left behind. The aorta arches over the top: its whole extent may be seen better in this view than in any other if it is sclerotic, but normally the outline of the lower border of the aortic arch is made out with great difficulty if at all. Below the aorta at the upper limit of the heart shadow posteriorly is the pulmonary artery. Between the aortic arch and the pulmonary arch is a clear space called the aortic window."

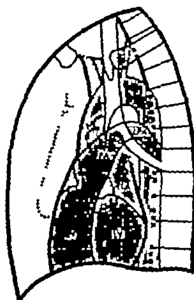


FIG. 27 Drawing of shadows of normal heart and great vessels in left anterior oblique position with various chambers and great vessels indicated. (Kindness of Sir John Parkinson and the *Lancet* London.)

PA, pulmonary artery
LPA, left pulmonary artery
LA, Left atrium
RV right ventricle
LV left ventricle

Note aortic window (open space) separating aortic arch from pulmonary arteries.

The chief advantage of the oblique views lies in the study of aorta and left atrium: this is especially true of the left anterior oblique view which has been regarded by some workers as the most valuable of all views in establishing the comparative size of the various parts of the heart.

Lateral view The lateral view is of value in measuring the depth, that is, the anteroposterior diameter of the heart for its own value or for use in a formula to estimate the heart volume (see page 146). This diameter is taken at right angles to the long axis of the heart.

Normal size of heart and great vessels. Certain measurements of heart size made on the orthodiagram or teleroentgenogram are in routine use and are of some value in spite of the wide normal variations and of the difficulty or

impossibility of judging accurately either the presence or degree of slight cardiac enlargement by such measurements It is obvious, for example, that increase in heart volume is represented by a far smaller increase in measurements of diameters or of area an increase of 100 cc of volume would add only about 15 sq cm to the area in the anteroposterior view

The following are the more useful teleroentgenographic measurements, all but two obtained in the anteroposterior view to make correction for orthodiagraphic records subtract 10 per cent. Other measurements of all sorts have been suggested but only the more important or interesting will be mentioned here.

The *transverse diameter* of the heart (T or H—Horizontal—of Bordet) is made up of the sum of the maximal distance of the right border from the midsternum (MR) and of the maximal distance of the left border from the midsternum (ML) Normally this diameter measures in the adult from 11 to 15 cm, depending on the size of the person, and from 6 to 10 cm in the child.

The *long diameter* of the heart (L) is the distance from the junction of right atrial and great vessel shadows on the right border to the point of the cardiac apex Normally this diameter measures in the adult 1 0 to 1.5 cm more than the transverse diameter on the average, therefore from 11 to 16 cm and in the child 0.5 to 1 0 cm more than the transverse diameter that is from 7 to 11 cm.

The *broad diameter* of the heart (B) is made up of the addition of the lengths of two perpendiculars dropped from the line of the long diameter to the junction of right atrial shadow and diaphragm on the right (BR) and to the junction of left atrial (or left ventricular) and pulmonary artery (or right ventricular) shadows on the left (BL) Normally this diameter measures in the adult 8 to 11 cm and in the child 5 to 8 cm

The *left ventricular chord* (LV or VG—*ventricule gauche*—of Bordet subtends the arc of the left ventricle from its upper extremity on the left to the apex. Normally this chord measures in the adult from 5 to 9 cm, and in the child from 3 to 5 cm.

Width of the great vessels (GV) A measurement of some interest but not of much value is that of the width of the shadow made by the great vessels at the widest part of the pedicle of the heart shadow usually at the level of the second intercostal space horizontally measured. This measurement varies not only with dilatation of the aorta and superior vena cava but also with kinking of the aorta when it is very tortuous from arteriosclerosis or pushed upward by an enlarged or horizontally placed heart resting on a high diaphragm. Normally the width of the great vessels measures 5 to 7 cm in the adult and 3 to 4 cm in the child of ten years of age.

The *diameter of the aortic arch* (Ao) taken in the anteroposterior position, is a measure of the length of the horizontal line drawn from the outermost bulge of the aortic shadow at the left of the midsternum to the shadow of the barium-filled esophagus, which, passing under the aortic arch, outlines

the right border of the descending portion of the arch a subtraction of 2 mm is necessary to take into account the thickness of the wall of the esophagus. If this line is not horizontal the measurement is inaccurate, because of abnormal relative positions of aorta and esophagus. The normal upper limit of this aortic arch measurement in the adult should not be over 3 cm The diameter of the aorta at the beginning of the arch (Ao or Asc A) is found in the right anterior oblique position by measurement of the horizontal line joining the two sides, the anterior edge outlined by the anterior mediastinum and the posterior edge by the trachea. Two millimeters comprising the thickness of the tracheal wall should be subtracted from this measurement to obtain the true aortic diameter which should normally range from 2.5 to 3 5 cm at this point. An unsatisfactory measurement of the diameter of the aortic arch is that obtained in the left anterior oblique position namely the vertical distance from top to bottom of the aortic arch shadow at the top of its curve. This in the normal adult averages 3 0 to 3 5 cm. It is unsatisfactory because often the lower border of the aortic arch is seen only with great difficulty if at all, unless a contrast medium has been injected.

The *depth of the heart* (or anteroposterior diameter) is measured at right angles to the long axis of the heart in the lateral view at the point of greatest thickness. Normally this measures two thirds to three quarters of the transverse diameter of the heart in the anteroposterior view (Roesler 1934) or in the adult 6.5 to 10.5 cm and in the child 4 to 7 cm. Its chief value is in checking the significance of the measurement of the diameters of the anteroposterior view and in forming a part of a formula for estimating the volume of the heart.

A standard but often unsatisfactory measurement of chest size for comparison with heart size is the *internal diameter of the thorax* (Th) at its widest point just above the diaphragmatic attachment.

The *area* of the heart shadow (A) which does not include the great vessels is measured after arbitrarily joining by slightly convex lines the outer and visible ends of the upper and lower borders. The area can be easily determined by the use of a planimeter less easily by superimposition of cardiac outline on paper specially ruled with centimeter squares, or by weight of paper cut out exactly to fit heart shadow compared to weight of 100 sq cm of the same paper (Mazer 1942) but most easily by nomogram based on the broad and long diameters of the heart (Ungerleider and Gubner 1942) The area of the normal heart shadow in the anteroposterior teleroentgenogram measures in the adult from 65 to 145 sq cm, averaging 112 for males and 100 for females, and in the newborn from 17 to 20 sq cm.

Finally attempts have been made to obtain a measurement of *heart volume* by the use of various formulas. Such measurement, theoretically ideal, has not as yet proved practical it will be discussed below The range of the normal heart volume in the adult male is from 400 to 900 cc and in the adult female from 300 to 550 cc (Comeau and White, 1939)

When the heart lies horizontally the transverse and long diameters become more nearly the same. A correction of the normal transverse measurement for

position has been suggested, based on the angle between the lines of these two diameters, and utilizing the surface area of the body for standard comparison. The smaller the angle and also of course the larger the surface area of the body the longer should be the transverse diameter Figure 28A shows the average normal measurements of the transverse diameter with these two variables charted, and Figure 28B shows the surface area of the subject in square meters calculated according to height and weight. This latter figure may also be used in calculating the normal vital capacity (see Chapter 10)

The relationship of depth or thickness of the heart to the size of the area and diameters on the frontal plane silhouette is of much interest and of fundamental importance. The flatter the chest, the less is the depth of the heart and the greater are the various frontal plane measurements the deeper the chest the smaller should be the frontal plane measurements of the heart (Roesler, 1934)

Calculation of normal heart measurements. The simplest, most practical and most reliable heart measurements are those of the *diameters*, transverse long, broad and anteroposterior (or depth) They are measured directly and usually with ease. The transverse diameter is the most useful of the diameters the anteroposterior the least used. Tables, slide rules, and nomograms (Hodges and Eyster 1926 Ungerleider and Gubner 1942 Kurtz, 1943) have been constructed for the calculation of the normal average transverse diameter according to height and weight for comparison with the actual finding in any given case (Figure 29) The range of normal varies from 10 per cent above to 10 per cent below this figure, a fact that materially diminishes the value of this as well as all other roentgen measurements as utilized at present (see Chapter 2)

A roentgen measurement of heart size very popular in the past but generally unreliable and unsatisfactory because of the extremely wide range of the normal (from 33 to 57 per cent) is the so-called *cardiothoracic ratio* or *heart-lung quotient* using a fraction in which the numerator is the transverse diameter of the heart and the denominator the internal diameter of the thorax; the normal range is from 0.33 to 0.55 Not only is the range of normal too wide because of the poor correlative standard of thoracic width (height and weight are preferable although also open to objection) but the cardiothoracic ratio has in addition the defect inherent in the transverse diameter which does not take into consideration the broad diameter of the heart, which may be considerably increased in mitral stenosis, for example, without increase in the transverse diameter There are, however rare persons of unusual build, short and light with wide chests, in whom the cardiothoracic ratio applies more accurately than do other formulas.

The other diameters, especially the long and the broad are useful as supplements of the transverse but are more readily considered in connection with area measurements, either made directly or by formula as in the nomogram in Figure 29

The measurement of the *area* of the heart shadow in the frontal silhouette,

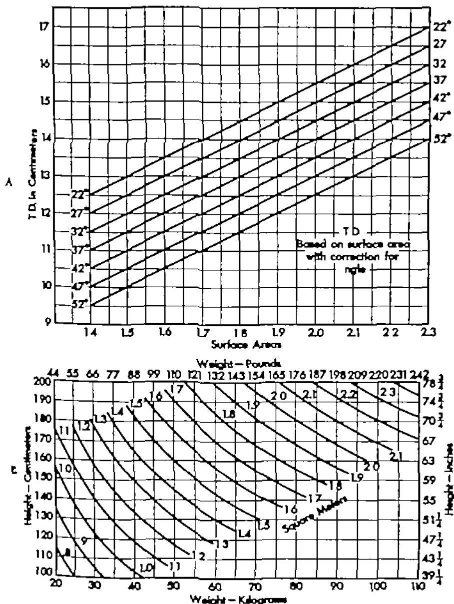


Fig. 28. Corrections for angle of heart' axis. (*A*) Chart for the determination of the normal variation of the measurement of the transverse diameter (T.D.) of the roentgen heart shadow with varying height and weight (Smith and Bloedorn, *U.S. Naval M. Bull* 1922, XVI, 219)

(*B*) Chart for the determination of the surface area of the body from the height and weight. (Dubois, E. F. Fig. 19 on page 119 of *Basal Metabolism in Health and Disease*, 2nd ed. Lea & Febiger Philadelphia, 1927

that is, on the usual anteroposterior teleroentgenogram or orthodiagram, i theoretically sounder than that of the diameters and actually it has bee found to be fairly satisfactory when compared to the size of the individu as in the formula *orthodiagraphic cardiac area in sq cm = age × 0.0204 + stature × 0.8668 + weight × 0.337 minus the constant 63.8049* (Hodges and

FIG. 29A. Nomograms for determination of the frontal area and transverse diameter of the normal heart shadow of teleroentgenogram and orthodiagram predicted from height and weight.

The Hodges Eyster formula applied by Kurtz. The roentgen films and orthodiagrams were made during quiet respiration. Add 10 per cent of patient s age to predicted transverse diameter The measurement of the area by teleroentgenogram is 11 per cent greater than the area of the heart shadow by orthodiagram. The transverse diameter of the heart shadow in the teleroentgenogram is 8 per cent greater than that of the orthodiagram.

In making the determination a straight edge joins the figures for the height and weight of given case. The points of intersection of this line with those recording area and transverse diameter are then read off as representing the expected verage area and, with the addition of 10 pe cent of the patient' ge, the expected verage transverse diameter An allowance of 10 per cent extra is to be considered the extreme upper limit of normal. (Kindness of Dr Chester M. Kurtz, Madison, Wis.)

Eyster 1924) Thus, for a person fifty years old, 173 cm (5 ft, 8 in.) tall and weighing 70 kg (154 lb) the orthodiagraphic cardiac area should be normally 112 sq cm. If the heart area is found to be 7 sq cm larger than the predicted area by this formula, the chances are 3 to 1 that the heart is actually enlarged; if the actual area is 14 sq cm larger than the predicted area, the chances of cardiac enlargement are 10 to 1 and if 21 sq cm larger the chances are 45 to 1 A simple calculation by slide rule or nomogram (Figure 29) can be made to determine the expected normal at any age, height, and weight, for either orthodiagram or teleroentgenogram.

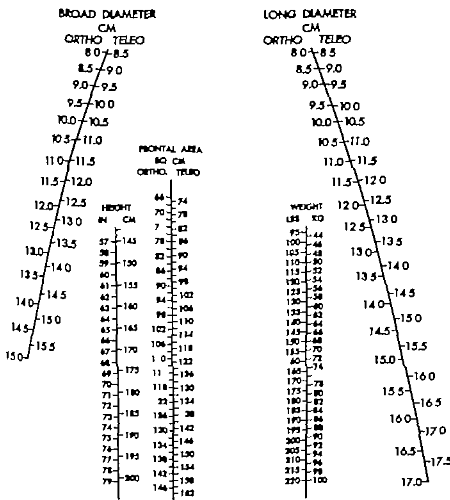


FIG. 29B. Area of heart shadow of orthodiagram and of teleroentgenogram determined from the long and broad diameters (the predicted area from height and weight) $A = \frac{\pi}{4} \times L \times B$. (Kindness of Dr Harry Ungerleider Equitable Life Assurance Society of the U.S New York City)

The ideal measurement of heart size by roentgen ray should be that of *volume* because of the established fact that the heart normally and abnormally varies considerably in all its diameters. As yet, however the determination of the heart volume has not been routinely introduced, and under present conditions it is not likely that it can be satisfactorily applied clinically for two reasons (1) in the first place there is far too wide a range of normal heart size using recognized correlations, and (2) the technic is not easy or accurate especially in the very cases of cardiac enlargement in which the physician is most interested. Various formulas have been suggested, especially those by Bardeen (1918) Kahlstorf (1932) Benedetti and Bollini (1934) and Strandquist (1935) Bardeen's formula is *0.53 × A (teleroentgenographic silhouette area)* $^{3/2}$ = *V (volume)* in a case with area of 100 sq cm, the heart volume would be calculated to be 530 cc by this formula which is probably not far from the true volume of a partially filled heart in an adult of average size. Kahlstorf's formula is *V (volume) = 0.63 × orthodiagraphic silhouette area of frontal plane heart shadow × maximum anteroposterior diameter (D)*. If the area in a given case equals 100 sq cm and the anteroposterior diameter equals 8.5 cm, the heart volume according to this formula would be 535 cc. Benedetti and Bollini have published a formula for the tridimensional heart size *Vc (vol) = 0 45 × the long diameter of the heart in the anteroposterior orthodiagram × the broad diameter of the heart in the anteroposterior orthodiagram × the depth of the heart in the lateral orthodiagram*, a case with long diameter of 12 cm transverse diameter of 10.5 cm, and depth of 9 cm would thus have a volume of 510 cc. Strandquist gives the following formula using orthodiagraphic measurements *V (volume) = 2/3 × 1/2 L (long diameter) × 1/2 B (broad diameter) × S (depth of heart in sagittal view)* using teleroentgenographic measurements he suggests *V = 0 42 L × B × S* Thus, using the last-named formula in the case of a normal adult with L = 14 B = 10 and S = 9 we find that V = 529 cc. One must, of course, correlate the heart volume determined by any formula to body size and also to the degree of filling of the heart under some standard condition. As has been noted already the filling of the heart and hence its volume will vary greatly under certain conditions, probably changing *at least 100 per cent in passing from the Valsalva* experiment to the Müller experiment (see page 135)

Careful clinical studies made at the Massachusetts General Hospital (Comeau and White 1939 and 1942) have demonstrated the inadequacy of all these various measurements, chiefly because of the wide range of the normal heart size and shape in connection with all recognized correlations, such as height and weight and body surface area. It is hoped that other standards representing types of body build may some day prove more suitable and permit more reliance on roentgen measurements. At present the simple transverse diameter of the heart related to body height and weight, following Hodges and Eyster's tables seems the most satisfactory measurement of heart size, with area a moderately close second. The reason why area is not better as it should be on first thought, is that a considerable part (the upper and lower

borders) of the circumference of the heart shadow (in the anteroposterior view) has to be arbitrarily completed before the measurement by planimeter can be made This same reason, plus the frequent difficulty of sharp measurement of the depth diameter of the heart (as well as the great range of normal) makes the volume calculation unsatisfactory The commonly used cardiothoracic ratio is in general too crude and its normal limits are far too wide how ever it can be useful in rare cases who are not tall but who have very wide chests.

Finally it has been suggested that, in addition to inspection of the size and density of the hilus shadows of the lungs in the anteroposterior heart shadow a *measurement of their breadth* be made. *This is much better done on the right side*, the measurement being actually that of the lower main branch of the right pulmonary artery Normally this hilus shadow measures 11 to 14 mm broad (average 13 mm) with the tube 1 5 meters away from thorax and screen. If it is over 15 mm broad it is abnormal.

Taken altogether these measurements of heart and aortic size should be interpreted very freely· they are probably better than no measurements at all when they are so interpreted. But when an attempt is made to fit each case within narrow so-called normal, standard limits, it is better to discard all measurements and to rely simply on general impressions and experience. Some physicians do this now and are as successful in diagnosis as are other physicians who rely on extensive tables or formulas.

Activity of the normal heart and great vessels as seen roentgenologically Normally the *atrial contractions* precede by a small fraction of a second (about 0.15 second) the contraction of the ventricles. Theoretically this interval is sufficient to allow the atrial contractions to be visible in fluoroscopic examination, but often this is not actually possible, the vigorous ventricular action coming so soon after that of the atria that they both seem to share but a single motion. If, however the atria are enlarged and vigorous, and very close attention is paid to the right atrial and left ventricular borders in the anteroposterior view or to the left atrial and left ventricular borders in the left anterior oblique view it is possible to distinguish a retraction of the atrial border ahead of the ventricular This separation becomes more and more obvious and marked with increasing delay in atrioventricular conduction, and in complete block the atrial contractions may be clear Often atrial fibrillation, weak or scant atrial contractions, or obscure outlines prevent any evidence of atrial action at all in fluoroscopic examination, and if there is free mitral or tricuspid regurgitation, ventricular systole may be vigorous enough to cause an outward movement of the atrial borders.

Ventricular action also varies very much normally in force, extent, and character In repose it tends to be quiet, slight to moderate in fullness, and slow with leisurely (that is, relatively long) systole. After exertion and with excitement it is active, rapid, and forceful, with shorter systole with the especial increase of circulation due to exertion the contractions are fuller as well as more rapid. In the upright position a vertical heart may beat rapidly and force

fully laboring to send out blood which is coming to it in too small an amoun *Firm abdominal pressure, by relieving this situation, slows and calms th* heart action. When the ventricles contract, apex and base of the heart ap proach each other the base moving down in this process even more than th apex moves up and the heart rotates to the right so that the apex of the le ventricle strikes the chest wall This composite movement is more obvious i the case of the horizontally placed heart than in that of the vertical heart. can be made more evident in either case by increasing the fullness of contra tion by exercise. The pulse of the ventricles is a single rapid process, n accompanied by a wave of contraction the wave-like change that is som times seen passing down over the base of the left ventricle with systole simply the actual movement of the base, that is, the atrioventricular junctio toward the apex as the heart contracts

The *great arteries* that is, the aorta and pulmonary artery are seen to dila with systole as the blood is pumped into them this results in a vertical rocki or seesaw motion of the heart shadow with retraction below and outthru above, especially evident along the left border This motion can be increase by exercise or excitement and in itself is not abnormal except as it may b much magnified under certain conditions, as, for example, with aortic or pu monary regurgitation. Pulsation of the great veins is not normally visible e cept for that of the superior vena cava in the recumbent position when atri and ventricular waves are seen. A slight pendulous movement of the heart due to respiration and not to heart action itself Moderate pulsation of the hi hiluses due to the presence there of the larger branches of the pulmona artery may be normally visible in thin adults or in children with increase heart action.

Roentgenkymography electrokymography and roentgencinematograph already described above, are methods that may be employed to obtain perma nent records of cardiac and vascular pulsation and thus to supplement fluoro scopy

ABNORMALITIES OF SIZE, SHAPE, AND ACTIVITY OF HEART AND GREAT VESSELS STUDIED BY ROENTGEN RAY

The various abnormalities of the roentgen shadows of the heart and great vessels will be presented in appropriate chapters later in the book with par ticular relation to etiologic types and structural defect. The index may be con sulted for quick reference to the special pages concerned. A few further notes should be added, however in concluding the present chapter

Disorders of cardiac rhythm Although it is possible to diagnose such dis orders of mechanism as premature beats paroxysmal tachycardia, atrial fibril lation and even flutter atrioventricular nodal rhythm, and heart block by fluoroscopy their identification and analysis are so much easier and more com plete by other methods of examination, especially electrocardiography that fluoroscopy is not a procedure of choice for their study Their presence may be first noted in roentgen ray examination, but details are sure to be missed

With tachycardia, whether of physiologic or pathologic nature, the heart shadow often decreases in size with bradycardia the reverse is usually true

Calcification. Calcification may be noted in *heart arteries* or *pericardium.* It is most commonly and easily seen in the peripheral arteries, especially in those of the legs. The tortuous course of the calcified vessels may be found with or without symptoms or signs of faulty circulation in muscles and skin, such as intermittent claudication or gangrene. The next most common site of visible calcification is the thoracic aorta, the whole vessel may be clearly outlined by general calcification (Figure 144 page 749) or there may be irregularities of density due to plaques. The abdominal aorta may also be sufficiently calcified to be visualized by roentgen ray especially if there is much air in the overlying gastrointestinal tract. Uncommonly there may be enough calcification of a diseased pericardium to be visible by roentgen ray (see Figure 140 page 730) such calcification is best noted, end on, in the oblique or lateral views. Sometimes calcified valves (especially in calcareous aortic stenosis) or areas in the myocardium (old infarcts) or even calcified mural thrombi may be seen. Calcified coronary arteries may be recorded on the roentgenogram or seen fluoroscopically but only in cases of advanced disease which is usually clearly evident on clinical examination here the calcification is simply a gravestone covering tissue long dead.

Pressure on bones Changes of bones due to erosion or deformity caused by heart or blood vessels are to be looked for A very large heart in early childhood may cause a bowing out of the left anterior chest wall. With coarctation of the aorta the ribs may be eroded by the widened intercostal arteries, a result of the attempt of the body to compensate for this congenital defect (see Figure 77 page 332) in some cases the diagnosis of this congenital defect has been first suggested by roentgen ray examination. Vertebrae, sternum, and ribs may be found to be eroded by the pressure from aneurysms of thoracic or abdominal aorta or of the main branches of the thoracic aorta.

Fat shadows. At the apex there is often a considerable triangle of fat lying in a fold between pericardium, pleura, and diaphragm (epipericardial fat) this is of less density than the heart shadow (see text and Figure 7 pages 38 and 39) and should not be confused with it to occasion an incorrect diagnosis of cardiac enlargement, such as has frequently happened (McGinn and White, 1936) This mass of fat may be as wide in transverse diameter as 2 cm It can be easily differentiated on fluoroscopy especially on deep inspiration, and by contrast films. There may be fat also at the right heart border but of lesser amount.

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CHAPTER 8

THE PULSATION OF HEART AND BLOOD VESSELS SPHYGMOGRAPHY BALLISTOCARDIOGRAPHY THE CAPILLARY CIRCULATION

Very little revision of this chapter has been needed for the present edition of this book. A brief section, however has been added on ballistocardiography for it is here that such mechanical recording belongs.

Harvey W *Exercitatio Anatomica D Motu Cordis Et Sanguinis In Animalibus.* Frankfurt-am-Main, 16_8 (*An Anatomical Disquisition on the Motion of the Heart and Blood in Animals.* Translation by Robert Willis for the Sydenham Society in 1847)

"Chapter I. The Author s Motives for Writing.

"When I first gave my mind to vivisections, as a means of discovering the motions and uses of the heart, and sought to discover these from actual inspection, and not from the writings of others, I found the task so truly arduous, so full of difficulties, that I was almost tempted to think, with Fracastorius, that the motion of the heart was only to be comprehended by God. For I could neither rightly perceive at first when the systole and when the diastole took place, nor when and where dilatation and contraction occurred, by reason of the rapidity of the motion, which in many animals is accomplished in the twinkling of an eye, coming and going like a flash of lightning so that the systole presented itself to me now from this point, now from that the diastole the same' and then everything was reversed, the motions occurring, as it seemed, variously and confusedly together My mind was therefore greatly unsettled, nor did I know what I should myself conclude, nor what believe from others' I was not surprised that Andreas Laurentius should have said that the motion of the heart was as perplexing as the flux and reflux of Euripus had appeared to Aristotle.

At length, and by using greater and daily diligence having frequent recourse to vivisections, employing a variety of animals for the purpose, and collating numerous observations, I thought that I had attained to the truth, that I should extricate myself and escape from this labyrinth, and that I had discovered what I so much desired, both the motion and the use of the heart and arteries; since which

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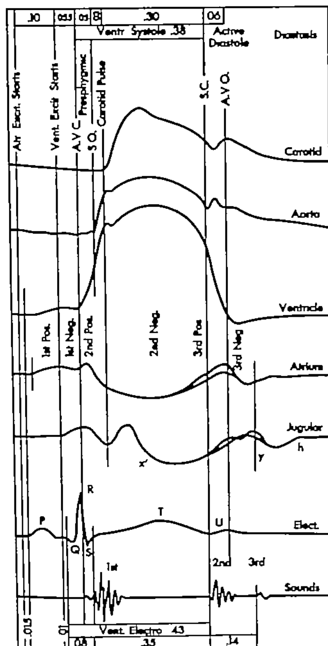


FIG. 30. Chart showing time relations of electrocardiogram, atrial and ventricular contractions, pressure changes, and heart sounds. (Lewis' *Mechanism and Graphic Registration of the Heart Beat.* Kindness of Shaw and Sons, Ltd., London.)

ence to the centre than in the opposite direction, were there even no valves to oppose its motion.

Sphygmography (σφυγμός, pulse, and γράφειν to write) is the process of obtaining a tracing of cardiovascular pulsation whether from the apex impulse of the heart (*cardiogram*) from brachial, radial, or other artery (*arteriogram*) from jugular or other vein (*phlebogram*) or from pulsating liver (*hepatogram*) The term polygram applies to simultaneous records of any two or more pulses or of pulse and respiration. Commonly the polygram registers the brachial or radial pulse and the jugular pulse in addition the electrocardiogram is usually recorded simultaneously or even replaces one of the other mechanical graphic tracings. The instrument which makes any of these combined tracings is called the polygraph. The technic of sphygmography will not be discussed in this edition it is amply presented elsewhere (see Bibliography at end of this chapter) It need only be added here that developments in the last few years have made it possible to obtain with ease excellent electrical (galvanometric) tracings of cardiac, arterial, and venous pulses (Miller and White 1941) that total cardiac vibrations recorded by the cathode ray are now available for study (Kountz and Smith, 1941) and that graphic records of the recoil of the body from the ejection of blood by the heart into the aorta (ballistocardiograms) have been utilized to estimate the cardiac output per beat (Starr et al. 1939 1940)

CARDIOGRAM

Although it may seem at first thought that records of the pulsation of the heart itself transmitted to the chest wall should be simple and reliable evidence for the analysis of the mechanism of the heart beat, experience has shown otherwise. The result is that the cardiogram is rarely obtained or studied except in special instances or in investigative work The reasons for this neglect are several. In the first place the technic is often far from easy A thick chest wall, pulmonary emphysema, or very weak heart action may make it difficult or impossible to find any cardiac impulse at all. In the second place, the shape and interpretation of the tracing depend on what part of the impulse is recorded, whether that over the left ventricle at the apex or that nearer the sternum over the right ventricle. In the third place, the complexity of the tracing, which is often difficult to explain, makes it less convenient than the arteriogram phlebogram, and electrocardiogram in the analysis of arrhythmias. And, finally in our present state of knowledge at least, more helpful information is afforded us by the other tracings, for example, slight pulsus alternans in the arteriogram shown poorly or not at all in the cardiogram, delay in atrioventricular conduction in the jugular phlebogram found with difficulty by direct cardiography and information about the myocardium shown by intraventricular block and T wave changes of the electrocardiogram and usually not even suggested by the cardiac apex tracing. Nevertheless, the cardiogram is of some individual interest for itself and should be briefly described

The normal cardiogram varies according to whether it is obtained over left ventricle or right ventricle (Figure 31) Over the left ventricle the outthrusts, and hence the upstrokes of the tracing, occur with systole over the right ventricle, unless it is enlarged, systole causes depression. If the atrial contraction is vigorous and tracing conditions favorable we may find a definite upstroke, a, preceding the sharp higher ventricular upstroke of the left ventricular apex impulse, or preceding in the same way the sharp ventricular downstroke over the right ventricle. This "a" wave is more prominent over the right ventricle than over the left, especially in the epigastrium. A record taken where systolic outthrust and retraction merge will show various and sometimes confusing combinations of the two tracing shapes. The wave due to ventricular contraction is usually overshot in the tracing, partly because of the actual event but also because of the varying degrees of inertia of the apparatus employed. Then follows during ventricular systole a settling down to a variable level till the shock of closure of aortic and pulmonary valves ends systole and begins diastole. Quite early in diastole (about a tenth of a second after its onset) there may appear coincident with a protodiastolic heart sound, a slight impulse, due probably to the vibration of the ventricular walls from the current of blood that enters at that time (Figure 31) Such a diastolic event is more likely to be recorded with forceful, slow heart action in thin young persons, or with serious protodiastolic gallop rhythm (discussed in Chapter 5) Finally various oscillations may appear in the cardiogram which are unexplained but are probably due to vibrations of the chest wall

Abnormalities of the cardiogram include increased and decreased force and excursion of the atrial and ventricular systolic impulses and retractions, delay between these impulses in heart block, and extra waves in gallop rhythm (see Figure 31)

Gross pulsatory movements of the wall of the thorax resulting from the heartbeat (Dressler 1937) have already been referred to in Chapter 5 page 69

ARTERIOGRAM PULSE WAVE VELOCITY

Arteriogram. An arterial pulse tracing may be obtained from almost any superficial artery but it is customary to use the brachial or radial artery for such a purpose. Nearly a century ago the first attempts were made to study the circulation in man in health and disease by tracings on smoked paper made by crude instruments attached to the radial artery (Vierordt, 1855 Marey 1860) Despite great expectations and extravagant interpretations the new records at first added little knowledge beyond that which had already been gained by mere palpation or inspection of the arterial pulse. As a result, sphygmography was abandoned for nearly half a century except for special studies. The technic and apparatus poor and difficult at first, slowly improved, due to these special studies, until with new discoveries concerning cardiac arrhythmias and alternation of the pulse the method was reintroduced into the clinic toward the end of the last century with far more success than at first.

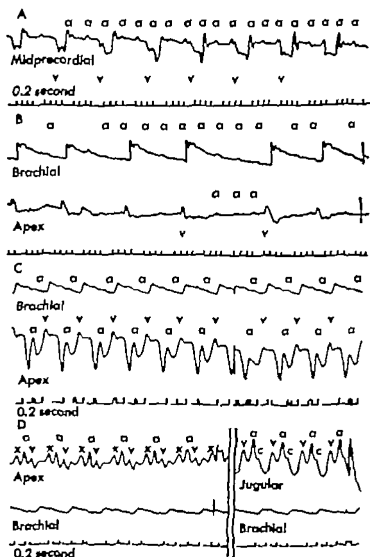


FIG. 31 Cardiograms showing (*A*) ventricular systolic negative ( ) and atrial systolic positive ( ) waves in case of complete heart block with the receiver placed over the precordium midway between the apex impulse and the lower end of the sternum, and hence over the right ventricle, (*B*) upstrokes with ventricular systole (v) and atrial systole ( ) in the same case of complete heart block represented in (*A*) but with the receiver at the cardiac apex, and hence over the left ventricle—note also the "a v ves in the brachial arteriogram taken simultaneously with the cardiogram (*C*) atrial (a) and ventricular ( ) upstrokes with the receiver at the cardiac apex in case with slight delay in a-v conduction, unusually vigorous atrial action, and presystolic gallop rhythm, and (*D*) three waves, a, and x representing atrial, ventricular and protodiastolic impulses with the receiver at the apex in case of congestive failure showing well-marked protodiastolic gallop rhythm without any delay in conduction (as proved by jugular phlebogram and electrocardiogram) Time interval = 0.2 second.

It was almost entirely the shape and amplitude of the tracings that had attracted attention at the beginning, rate and rhythm being largely ignored until many years later The various shapes of tracings of the arterial pulse were prominent in the textbooks of the day and it was hoped that they might prove more useful than they did. We realize now that the shape and amplitude of the arteriogram are complicated not only in themselves but frequently also by the addition of artifacts due to the graphic method itself. By the employment of more accurate apparatus the distortion can now be avoided.

The normal arterial pulse wave The arteriogram consists of a graphic record of a series of pulse waves in an artery It should be of normal rhythm and rate (40 to 100 per minute, at rest usually 60 to 80) The normal pulse wave (Figure 32) shows at first a sharp upstroke rising a variable distance from the baseline, the amplitude depending on the fullness of the pulse and the sensitiveness of the recording apparatus. Vibrations may be found on the upstroke if the curve is taken by the use of the Frank capsule, crystal microphone and galvanometer or cathode ray· such vibrations are called anacrotic (ἄνω, up, and κρότος, stroke) The upstroke is quickly succeeded by a short, sharp fall to a notch, called the predicrotic (πρὸ before, δὶς, second, and κρότος, stroke) resulting from the artifact of overshooting or fling due to instrumental inertia. The distance from the peak of the wave to the predicrotic notch varies according to two factors, the amount of inertia of the recording apparatus and the fullness of the pulse the more of each of these, the greater the distance. It is not always possible to make out this notch it may be buried in the rapid decline to the dicrotic notch, especially where there is a water-hammer or hyperdicrotic pulse shape. Following the predicrotic notch appears the curved systolic decline, ending as a rule abruptly at the dicrotic notch, which represents the time of aortic valve closure and second heart sound. The time interval from beginning of the main upstroke to the dicrotic notch (usually 0 25 to 0.35 second depending on the pulse rate) represents the duration of systole minus the so-called presphygmic (πρὸ before, and σφυγμός, pulse) interval, which is the time at the beginning of systole after the closure of the mitral and tricuspid valves (time of first sound) when intraventricular pressure is rising but not sufficiently to raise the aortic cusps and start the pulse wave along the aorta, this presphygmic interval or isometric (ἴσος equal, and μέτρον measure) phase is very short (calculated variously as 0 04 to 0 08 second) The dicrotic notch is followed by the dicrotic wave, usually a slight convexity upward due to the rebound of the pulse wave at the closure of the aortic cusps. This gives way to a gradual fall of the baseline to the next systolic upstroke Rarely a very small additional wave ("a) occurs, just preceding the systolic upstroke due to the effect of atrial systole on intraventricular and aortic pressure. Finally when more accurate tracings are obtained, as already mentioned, additional oscillations, for example, on the systolic upstroke, may be seen, doubtless due to vibrations of the artery wall, their recording is not of any practical significance in the present state of our knowledge, but may perhaps be found to be of some importance by future studies.

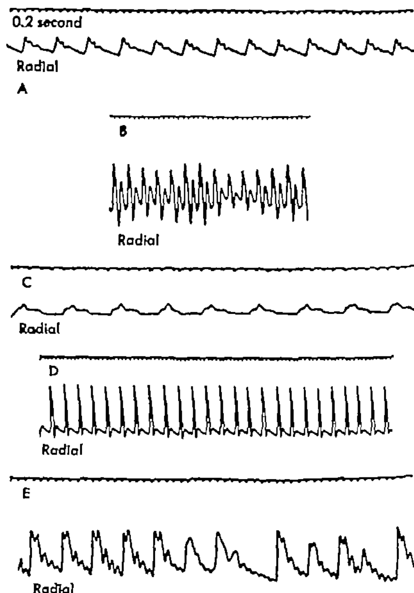


FIG. 32. Arteriograms showing various shapes of pulse curves with normal rhythm. (*A*) Normal average shape of arterial pulse wave showing upstroke, predicrotic notch (due to artifact of overshooting from inertia of instrument) and dicrotic notch and wave (due to closure of aortic valve)—the duration of systole is equivalent to the interval from the beginning of the upstroke to the dicrotic notch plus a small time interval representing the presphygmic period (see text). (*B*) Hyperdicrotic pulse in infection, showing exaggeration of the dicrotic notch and wave. (*C*) Plateau and anacrotic pulse of aortic stenosis. (*D*) Water-hammer pulse of aortic regurgitation. (*E*) Deformity of radial arteriogram due to oscillations caused by paralysis agitans. Note the two ventricular premature beats. Time interval of these and succeeding arteriograms and polygrams = 0.2 second.

Abnormalities of the arterial pulse wave in shape and amplitude Slight changes in shape and amplitude of the arterial pulse wave from the average normal are so generally found in arteriograms or are so easily caused by the procedure of registration itself that only well-marked variations, such as can be palpated in the radial pulse, should be considered here. Great increase in pulse pressure, that is, true increase in artery fullness, is not always easily apparent either on palpation of the arterial pulse or in the arteriogram. Its detection is dependent on relative emptiness of the artery in diastole along with increase of pulse pressure, but the diastolic laxness of the vessel is more essential than is increase in pulse pressure

Various abnormalities of shape and amplitude found in the arteriogram are illustrated in Figures 32 and 33

The most important by far of these abnormalities is *pulsus alternans* which consists of alternating fullness of pulse and of systolic and pulse pressure during normal heart rhythm, the result of weakness (generally serious) of the left ventricle (see Chapter 30) An interesting variation, abnormal and diagnostic (usually of acute or chronic constrictive pericarditis) when of high degree, is the *pulsus paradoxus* which consists of waxing and waning of the pulse volume (and pressure) with expiration and inspiration respectively in contrast to the usual increase of the pulse fullness during inspiration and its decrease during expiration in the case of normal diaphragmatic breathing; in marked instances the radial pulse may entirely disappear during inspiration (see Chapters 6 and 27) The various arrhythmias will not be illustrated here because they are so much better shown in electrocardiograms (see Chapters 32, 33 and 34)

Velocity of the arterial pulse wave. Quite aside from form and rhythm of the pulse and speed and volume of blood flow is the measurement of the velocity of the arterial pulse wave. This has been estimated in various ways, most simply by measuring the time interval between the appearances of the carotid and radial pulse waves graphically recorded simultaneously and dividing this time interval into the difference in centimeters between the distances from the heart of the recording points on the two arteries. This gives roughly the speed of travel of the pulse wave in centimeters per second. More accurate methods for making this measurement have been in recent years introduced, such as that of the use of the hot wire sphygmograph, which is an instrument transforming into variations of an electric current, recorded by galvanometer the air pressure waves transmitted from a pulsating vessel or from the heart through a tube past a fine spiral of platinum wire heated by the electric current, whose variations are recorded, the ends of this wire being connected with the galvanometer Normally the pulse wave velocity in the brachial and radial arteries has been found to be 5 to 9 meters per second, averaging about 7 meters. It is increased in hypertension and arteriosclerosis, and decreased in hypotension, aortic stenosis, and aortic aneurysm. It varies roughly with the speed of blood flow but it has little or no relation

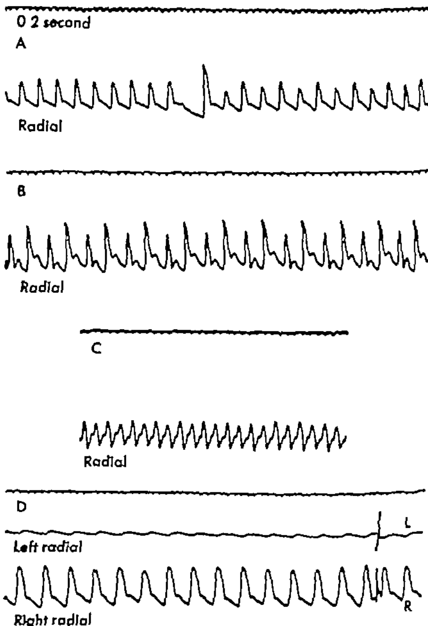


FIG. 33 Arteriograms showing pulsus alternans and unilateral pulse deformity due to aneurysmal obstruction. (*A*) Ventricular premature beat with compensatory pause followed by slight to moderate alternation of the pulse. (*B*) Constant pulsus alternans showing delay in appearance of alternate weak beats. (*C*) Pulsus alternans during a paroxysm of tachycardia (rate 185 per minute) (*D*) Diminished and delayed left radial pulse w ves due t aortic aneurysm with obstruction at the mouth of the left subcla ian artery

to volume of blood flow The measurement of the velocity of the pulse wave is not of much clinical value.

PHLEBOGRAM. HEPATOGRAM

Phlebogram (φλέψ vein, and γράμμα, inscription) The phlebogram, or graphic record of the venous pulse, is routinely obtained from the jugular vein. Although on rare occasions pulsations may be easily visible in other superficial veins, as in the arms, the jugulars as a rule are the only veins that show enough pulsation to give a satisfactory record this is due to their large size and close proximity to the heart. Venous pulsation has been known for centuries but it was not until the latter half of the last century that the development of the sphygmograph permitted the taking of actual tracings (Friedreich, 1866 Potain, 1867) and serious study of these venous pulse tracings did not begin until stimulated by a curiosity concerning the clinical significance of variations of this pulse (Mackenzie, 1893) Gradually by comparing the phlebogram thus obtained with cardiac or arterial pulse tracings, it became possible to recognize although not completely to explain, the various waves of the normal jugular pulse, and to describe certain ob-normalities.

In the clinic for a while the analysis of disturbances of the cardiac mechanism, like partial heart block, was chiefly dependent on the study of the polygram, which consisted of simultaneous jugular and arterial pulse tracings. But the frequently difficult and bothersome technic and the obscurity concerning interpretation in the minds of most physicians prevented a wide adoption of the method, doctors remaining content to continue for years the old custom of labeling irregularity of the heart rhythm as slight, moderate or marked. Eventually the interest of younger workers and especially the introduction of the practical electrocardiograph, the string galvanometer into the field of internal medicine resulted in the clinical applications of the lessons about cardiac mechanism first studied in the phlebogram by pioneers. The electrocardiogram gives information about the cardiac mechanism which is so much more accurate and complete than that given by the phlebogram, and the technic of securing the electrocardiogram and its interpretation when obtained are both so much easier that the phlebogram has been almost completely abandoned. However as in the case of the arteriogram, help can still sometimes come from the phlebogram. To represent graphically what one can see of jugular pulsation aids in understanding the mechanical evidences of cardiac action and is good training. Also, in certain cases when the electrocardiograph is not available and one deals with arrhythmias difficult to analyze without knowing how the atria are acting, the phlebogram may solve the problem. And even when an electrocardiogram has been secured, the question as to whether atrial waves are isoelectric or buried in ventricular waves may be answered by a study of the phlebogram. The jugular pulse tracing gives something the electrocardiogram cannot give, that is, mechani-

cal evidence of action of the heart chambers moreover certain abnormalities of the jugular pulsation may reveal cardiac insufficiency even when the electrocardiogram is normal. In addition, one can by electrical recording now obtain phlebograms with greater ease and accuracy than was possible in the past (Miller and White, 1941)

The normal and abnormal jugular phlebogram. Although proof does not exist for every detail of the interpretation of the normal jugular pulse tracing, the phlebogram is understood sufficiently to permit fairly full analysis. With each cardiac cycle there are normally three, four five or even six waves in the jugular pulse. Interpretation by inspection of these waves, especially if there are more than three, may prove to be very confusing. Therefore, although it is at times possible to see and to identify the three normal waves, or in the case of abnormalities to make correct analyses, there are so many variations that, in spite of much experience, interpretation by inspection of the vein is far less reliable than interpretation of the phlebogram itself.

There are three main waves in the jugular pulse (Figure 34)

The first wave due to atrial systole, has been routinely called the *a* wave. It can be identified only indirectly after the other two main waves (which are of ventricular origin) have been accurately measured off as a rule it precedes the second or *c* (ventricular systolic) wave by one fifth of a second, and it is variable in size depending chiefly on the posture of the subject, the force of the atrial contraction, and the degree of dilatation of the jugular vein. Other factors which influence the size of the *a* wave normally are instrumental technic and the fullness of blood flow With poor technic, for example by the application of too much pressure so that the vein is nearly collapsed or by holding the receiver somewhat away from the optimum position, the *a* wave of the phlebogram may be small and poorly defined. With increased heart action the *a* usually increases in amplitude and with increased circulation associated with increased blood volume, such as may temporarily result from the ingestion of a large amount of fluid, the *a* wave may also increase in size. It is biggest of all in cases of marked tricuspid stenosis with normal rhythm. It is ordinarily a single wave, a rounded upstroke rising sometimes at the peak of the jugular pulse, sometimes low near the baseline, and sometimes at midlevel, its position depending on the speed of the pulse, on the degree of stasis in the vein and on the relative submergence of the *a* in the ventricular systolic wave. The slower the pulse or the more congested the vein, the more the *a* wave tends to appear at the top of the curve. The faster the pulse, the less the congestion, and especially the more the systole of the ventricles is emphasized in the tracing, the lower lies the *a* wave. Although the *a* wave appears normally to be a single wave, this appearance may be in part due to the immediate succession of the ventricular systolic wave which conceals any other portion of the *a* wave. When there is a delay in atrioventricular conduction, partial or complete sufficient to separate clearly atrial and ventricular waves, the *a* wave sometimes appears doubled

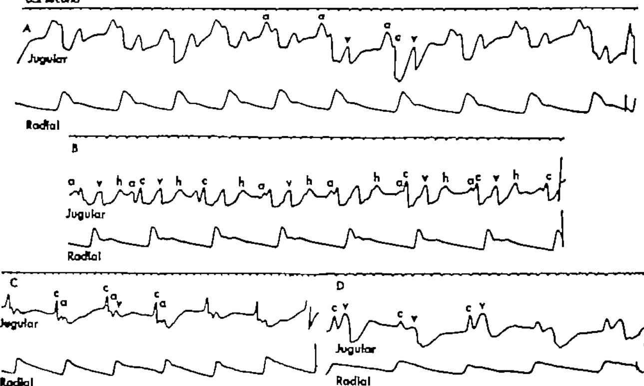


FIG. 34. Polygrams showing the jugular phlebogram in (*A*) normal sinus arrhythmia (= atrial, = ventricular and = stasis waves) (*B*) sinoatrial bradycardia with *h* waves (see text) in addition to the and waves (*C*) atrioventricular nodal rhythm in which the atrial contraction follows the ventricular as shown by the interpolation f the *a* wave between the and waves; and (*D*) atrial standstill in which condition no waves are seen either between or with the regularly recurring *c* and *v* waves.

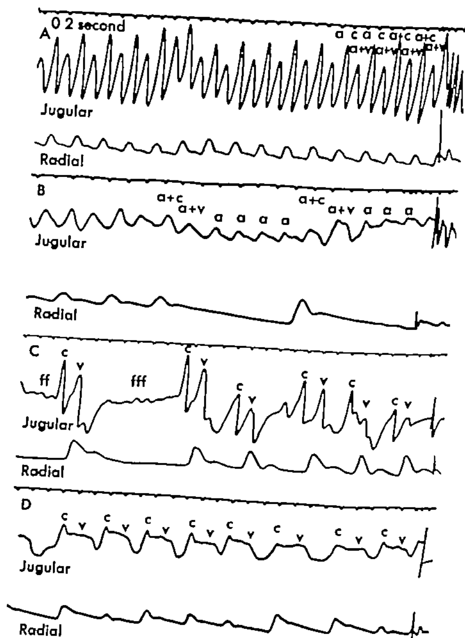


FIG. 35 Polygrams showing the jugular phlebogram in (*A*) trial flutter with two to one -v block (= atrial, = ventricular and = stasis waves) (*B*) atrial flutter with varying and higher degrees of block, the waves being clearly evident between the waves (*C*) atrial fibrillation with no *a* waves but with oscillations (*fff*) due to the irregular atrial contractions and (*D*) atrial fibrillation with the so-called "ventricular or better designated congestive" type of venous pulse due to coalescence of *c* and waves resulting from stasis.

or at least notched (Figure 36). Various abnormalities of the jugular phlebogram are illustrated in Figures 34, 35, and 36. Arrhythmias are not presented, because of their better analysis by electrocardiography (Chapters 32, 33 and 34) except as they illustrate particular points concerning the venous pulse tracing.

The a-c interval. The atrial wave of the jugular pulse tracing precedes normally that due to ventricular systole by 0.15 to 0.20 second; if there is a greater time interval (measured from the beginning of the *a* upstroke to the beginning of the *c* upstroke) atrioventricular block is present.

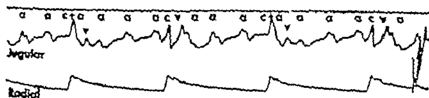


FIG. 36. Polygram showing the jugular phlebogram in complete atrioventricular block with complete dissociation of and waves. Note bifid *a* waves. Size reduced.

Following the first, or *a*, wave of the normal jugular phlebogram by the time interval just noted above appears the second, or *c*, wave, which is due to ventricular systole. It was labeled *c* because it was attributed to the pulsation of the carotid artery lying under the jugular vein. Undoubtedly the carotid pulsation does play an important part in its production but this part is variable in degree. In the venous pulsation itself there is a ventricular systolic wave transmitted up from the right atrium by way of the superior vena cava. This wave, together with that due to the carotid pulsation, forms the upstroke *c* of the jugular phlebogram, a positive wave of varying amplitude whose size depends upon a number of factors. The greater the carotid element of the *c* wave, the higher and more preponderant is this wave, and vice versa. There is one type of patient with mitral stenosis with greatly exaggerated c (and v) waves of the jugular pulse itself that deserves special mention. This pulsation concerns the deep jugular veins on both sides of the neck, but especially the right one. Because as a rule atrial fibrillation is present in these patients with no *a* waves in the phlebogram, because the pulse is so vigorous, and because it is so deep in position in the neck, it is easily and commonly confused with the carotid pulse (White and Cooke, 1939). It is due to tricuspid regurgitation with relatively little constant congestion or stasis, so that the pulse wave is propelled vigorously by right ventricular systole through tricuspid valve, right atrium, and superior vena cava into the jugular veins; it is easily obliterated by slight pressure over the jugular bulb. As a rule tricuspid valve deformity with stenosis is present in these cases of such pulsation of long standing, but in rare instances there is chronic irreversible dilatation of the tricuspid ring without valve deformity.

The *c* wave itself is identified by comparative measurement from the upstroke of the pulse wave of the brachial or radial arteriogram, or of the *QRS*

wave of the electrocardiogram, which is taken simultaneously with the jugular phlebogram for this very purpose Measuring back from simultaneous time lines of both tracings, established by allowing the pens each to write a stroke with the recording surface at rest, the beginning of the upstroke of the *c* wave will be found one tenth of a second earlier than the upstroke of the radial pulse wave or 0 135 second later than the *QRS* wave, this difference in time being that interval required for the pulse wave to travel a length of artery equivalent to the difference between the distances of the radial pulse and of the jugular pulse from the heart in the first instance, and to the sum of the travel time from the heart to the jugular bulb and of the electrical presphygmic interval in the second instance (see Figure 31 page 158)

The *c* wave may be found to occur irregularly rapidly or slowly and to be of varying shapes and amplitudes, but these characteristics of the arterial pulse and of heart action are better studied in the arteriogram itself as already discussed, or in the electrocardiogram.

The third main wave the *v* wave, of the jugular phlebogram is due primarily to stasis, that is to the gradual accumulation of blood in right atrium, superior vena cava, and jugular bulb at the close of ventricular systole. This stasis ends rather abruptly in a rounded peak and downstroke when diastole begins and the blood flows down into the right ventricle from atrium, vena cava, and jugular bulb It has been called routinely the *v* wave for ventricular systole, but a more correct expression might have been *s* for stasis, while the *c* wave might better have been called the *v* wave. However the firm establishment and the partial correctness of these designations warrant their retention. A second factor besides stasis, which has been suggested as in part responsible for the *v* wave is the rebound or return upward of the base of the heart at the beginning of diastole We do not know the relative importance of the two elements (the rebound and the stasis) or whether the frequent splitting of the *v* wave which is unexplained, can result from their difference in time (the diastolic rebound effect being later than the other) but evidence strongly supports the conclusion that stasis and not diastolic rebound is the essential cause of the *v* wave. The amplitude of the *v* wave varies as does that of the *a* wave and as a rule inversely as that of the *c* wave It is dependent to an important degree on the amount of venous stasis. If there is much stasis the *v* wave is more prominent if the stasis is extreme in degree there appears a characteristic variation consisting in a merging of *c* and *v* waves in one broad plateau with slight elevations at the ends and variable concavity between (Figure 35) This type of jugular pulse was once called the "ventricular" type, apparently because it was so often found in atrial fibrillation with absence of *a* waves. But it may be found with normal rhythm and *a* waves. It is due to congestion and so it may better be called the "congestive" type of jugular pulse.

The *v* wave is determined in its position in the jugular phlebogram by correlation with the radial arteriogram simultaneously recorded. Measuring back from synchronous points we find that the dicrotic notch of the arterial

pulse coincides with the peak of the *v* wave, though sometimes it may fall between the two peaks of the *v* Actually the dicrotic notch of the radial pulse represents closure of the aortic valve, an earlier event by 0 05 to 0 1 second than the opening of the tricuspid valve which is responsible for the beginning of the downstroke of the *v* wave. But since the pulse wave takes almost 0.1 second longer to reach the wrist (or slightly less time to reach the elbow) than to reach the base of the neck, these two events can be measured off together in the polygram.

One further wave may be found infrequently in the jugular pulse tracing, especially with slow forceful heart action. It is a small wave in diastole called the *h* or *b* wave (Hirschfelder 1907 Gibson, 1907) It is related to the preceding ventricular systole and not to the succeeding *a* or *c* waves which it may closely approach in time if the pulse is fast. It has been ascribed to the same mechanism that produces the normal third sound of the heart or the abnormal extra sound in protodiastolic gallop rhythm, but its timing sometimes appears late for this. It is not well understood, further study is needed to explain it. Whatever its mechanism, it does not at present appear important, except that its existence should be recognized so that it will not be confused with other waves (Figure 34) The *a* and *h* waves are located by a process of exclusion after the *c* and *v* waves have been identified.

What has been termed a second stasis or second onflow wave is the gradual movement upward of the baseline of the jugular phlebogram late in diastole just prior to the *a* wave it is prominent if there is bradycardia or congestion.

An interesting phenomenon which sometimes interferes with smooth recording of the jugular pulse is the paradoxical inspiratory filling in cases of venous hypertension (Hitzig, 1942) this has been discussed in Chapter 6 page 120. It emphasizes the need, well known to those experienced in phlebography to obtain, for their smoothness, records taken during held respiration, that is, held in whatever phase brings out the pulse waves to the best advantage.

An esophageal tracing of the left atrial pressure changes (esophagocardiogram) shows three waves, usually corresponding to the *a c* and stasis waves of the jugular pulse tracing: the *a* and *c* waves may be inverted if the receiver (a capsule filled with air) lies directly over the left atrium, for the atrium recedes when it contracts, as does the left ventricle. This method, however is an impracticable and unnecessary one.

Hepatogram (ἧπαρ, liver and γράμμα, inscription) A brief discussion of the liver pulse remains. A true perceptible liver pulse, not due to directly transmitted systolic movement of the liver by heart, aorta, or aneurysm, is uncommon. The reason for this is that the liver is so sponge-like that it absorbs much blood and much pulsation before it becomes sufficiently influenced actually to cause a visible, palpable, or traceable pulse. Slowly progressive chronic pericarditis or heart failure, although resulting in much hepatic enlargement with some fibrotic change and ascites, does not cause liver pulsation. Three factors are responsible for this pulsation (1) rapid, acute congestion with failure and functional tricuspid regurgitation, (2)

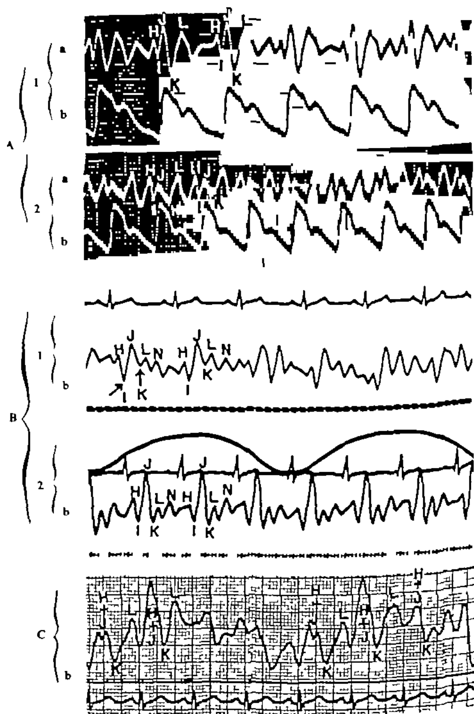


FIG. 38. Ballistocardiograms. (*A* 1) Normal curve. Male, age 34. Tracing shows normal waves H to K (period of cardiac ejection). Amplitude of J and K roughly approximate clinical measure of the stroke volume of the heart (*a*, ballistocardiogram; *b* arteriogram). (*A*) During acute rheumatic carditis. The J and K waves are of

Rheocardiogram. The changes that occur in the body's electrical resistance with each heartbeat can also be recorded electrically by connecting electrodes on right arm and left leg to alternating current of high frequency (10 000 to 50,000 oscillations per second) Measurement of electrical impedance of the body is not new: in 1937 Mann stated "When the electrical conductivity of any part of the body is measured by means of an alternating current bridge it is found that this conductivity shows a rhythmic variation synchronous with the pulse. The curve, which has been called an electrical plethysmogram, ascends with increase in body resistance during systole when the heart volume decreases relative to the lung air volumes on either side and descends when diastole begins. In myocardial failure with prolongation of the isometric period the descent of the curve is delayed and with mitral regurgitation the ascent is slowed (Holzer and Polzer 1947) Complete inversion of the curves has been reported in cases with extensive edema, with reversal when the edema cleared (Weissel, 1948) This technic has not, however been adopted routinely in clinical practice: further investigation is needed even to determine whether or not it has any value as a research tool. Recent work has indicated its possible value in the study of the peripheral circulation (Nyboer 1950) where it may act as an electrically recording plethysmograph.

CAPILLARY CIRCULATION AND PULSATION

It remained for Malpighi in 1661 to complete the proof of the circulation of the blood presented by Harvey in 1628 Harvey had postulated that "in the limbs and extreme parts of the body the blood passes either immediately by anastomosis from the arteries into the veins, or mediately by the pores of the flesh, or in both ways, as has already been said in speaking of the passage of the blood through the lungs." Only in recent years has the existence of direct anastomoses between arteries and veins been demonstrated (Grant, 1931 Grant and Bland, 1931) but the "pores of the flesh" or capillaries were discovered in the lungs by Malpighi.

Malpighi in a letter to Professor Alphonsus Borellius of Pisa describes his discovery of the pulmonary capillaries. (*D pulmonibus observationes anatomicae*, Bologna, 1661 translated by James Young, M.D *Proc Roy Soc Med.*, 1929–1930 XXIII, 7–11 Part I.)

low amplitude with relatively tall H and L waves (*a*, ballistocardiogram *b* arteriogram) (Kindness of Dr. William Dock, Brooklyn, N Y)

(*B* 1) Ballistocardiogram and electrocardiogram of case of coarctation of aorta before operation showing relatively small J waves and very small K wave. The arrows point to the short J and K strokes characteristic of coarctation of the aorta (*a*, electrocardiogram; *b* ballistocardiogram) (*B*) Same case after operation, the J and K waves are now normal (*a*, electrocardiogram, *b* ballistocardiogram) (Kindness of Dr Herbert R. Brown, J Rochester N Y and *New England J Med*)

(*C*) Case of angina pectoris, A.D male, age 49 Note respiratory effects but in particular the fusion and, or notching of the H and J waves (*a*, ballistocardiogram; *b* electrocardiogram) (Kindness of Dr William Dock, Brooklyn, N Y)

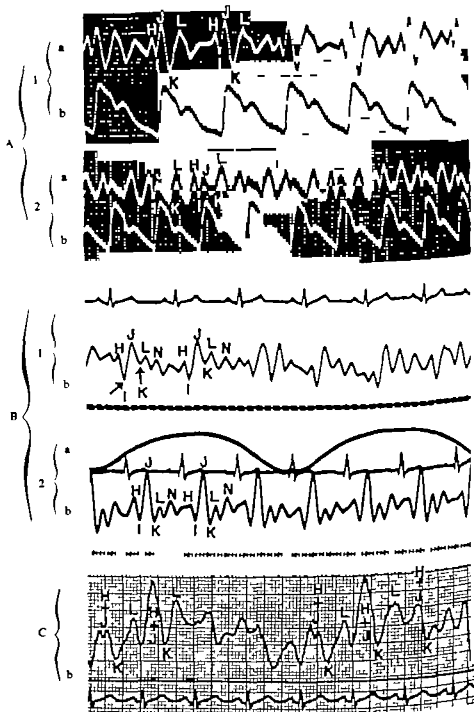


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And now most famous man, I will handle the matter more closely There were two things which, in my epistle about observation on the lungs, I left as doubtful and to be investigated with more exact study

(1) The first was what may be the network described therein, where certain bladders and sinuses are bound together in a certain way in the lungs.

(2) The other was whether the vessels of the lungs are connected by mutual anastomosis, or gape into the common substance of the lungs and sinuses.

"The solution of these problems may prepare the way for greater things and will place the operations of Nature more clearly before the eyes. For the unloosing of these knots I have destroyed almost the whole race of frogs, which does not happen in that savage Batrachomyomachia of Homer For in the anatomy of frogs, which, by favour of my very excellent colleague, D Carolo Fracassato, I had set on foot in order to become more certain about the membranous substance of the lungs, it happened to me to see such things that not undeservedly I can better make use of that (saying) of Homer for the present matter—

" I see with my eyes a work trusty and great

"For in this (frog anatomy) owing to the simplicity of the structure, and the almost complete transparency of the vessels which admits the eye into the interior things are more clearly shown, so that they will bring the light to other more obscure matters.——

"Observation by means of the microscope will reveal more wonderful things than those viewed in regard to mere structure and connection for while the heart is still beating, the contrary (i.e., in opposite directions in the different vessels) movement of the blood is observed in the vessels,—though with difficulty—so that the circulation of the blood is clearly exposed. This is more clearly recognized in the mesentery and in the other greater veins contained in the abdomen.

"Thus, by this impulse, the blood is driven in very small (streams) through the arteries like a flood into the several cells, one or other branch clearly passing through or ending there. Thus the blood, much divided, puts off its red colour, and, carried round in a winding way is poured out on all sides till at length it may reach the walls, the angles, and the absorbing branches of the veins.

"The power of the eye could not be extended further in the opened living animal, hence I had believed that this body of the blood breaks into the empty space, and is collected again by a gaping vessel and by the structure of the walls. The tortuous and diffused motion of the blood in divers directions, and its union at determinate place offered a handle to this. But the dried lung of the frog made my belief dubious. This lung had, by chance, preserved the redness of the blood in (what afterwards proved to be) the smallest vessels, where by means of a more perfect lens, no more there met the eye the points forming the skin called Sagrino but vessels mingled annularly And, so great is the divarication of these vessels as they go out, here from a vein, there from an artery that order is no longer preserved, but a network appears made up of the prolongations of both vessels. This network occupies not only the whole floor but extends also to the walls, and is attached to the outgoing vessel, as I could see with greater difficulty but more abundantly in the oblong lung of a tortoise, which is similarly membranous and transparent. Here it was clear to sense that the blood flows away through the tortuous vessels, that it is not poured into spaces but always works through tubules, and is dispersed by the multiplex winding of the vessels.——

Physiologic studies of the capillary circulation have in late years attracted much attention and have revealed new facts of some importance (Krogh, Lewis, Lombard, Richards, Crawford, Landis) but in routine or even in special cardiovascular examination they have not yet proved important. The reasons for this are two In the first place, but few capillaries in man can be studied and these are at the body surface best seen at certain localities like the nail beds and subconjunctiva (and with difficulty in the eye grounds) In the second place, great variations of capillary conditions exist not only throughout the body at a given moment, but even in a single area at different moments, due to the frequent periods of changing activity (dilatation) and rest (contraction) characteristic of arterioles and body capillaries in general. Thus capillary findings at a given moment in a given area may be very dif ferent from those in many other areas or in the same area at a different time. There are, however certain clinical facts of interest determined by scrutiny of skin capillaries by microscope through the intervention of oil and the use of reflected light for illumination (Lombard, 1912) In cyanotic states, as in some cases of congenital heart disease with polycythemia, or in one of the phases of Raynaud's disease, capillaries of the fingers are widely dilated while the blood stream through them may be sluggish, normal, or rapid, according to the state of the arterioles. In conditions of pallor as in another phase of Raynaud's disease, the capillaries and arterioles are constricted and the blood stream is slowed. The ingenious studies by Crawford (1926 1927) and Landis (1930 1934 1938) have revealed interesting facts about the structure and action of the capillaries and concerning capillary blood pressure and perme ability

Capillary pressure. Landis (1930, 1934 1938) by microinjection measured directly and studied the mean blood pressure in the capillaries of the human skin at the base of the finger nail. He found the average pressure in the ar teriolar limb of the capillary to be 32 mm of mercury at the end of the loop 20 mm, and in the venous limb 12 mm. "The fall of blood pressure does not cease at the junction of the arterioles and capillaries, he wrote, "but con tinues unbroken through the capillary loop Average blood pressure in the arteriolar limb is above and in the venous limb below the osmotic pressure of the plasma proteins. These direct pressure readings in human capillaries are in agreement with Starling's hypothesis of fluid balance. Landis further found that hyperemia due to heat was attended by a doubling of the capillary blood pressure. Elchna and his associates (1942, 1943) have shown that, despite the fact that pressure in the capillaries of the digits falls somewhat with arteriolar constriction and rises somewhat with increase in venous pressure, there is a surprising degree of constancy in the digital capillary pressure during wide fluctuations in digital blood flow Eichna (1943) reported his finding of the average digital capillary blood pressure in human fingers with intact innervation to be 18.5 mm of mercury in the arteriolar limb (summit, 22.4) and 19 mm in the venous limb. Recently Pappenheimer and Soto-

Rivera (1948) have further confirmed the concept that capillary pressure and colloid osmotic pressure are in balance by measuring the rate of filtration of fluid from blood to tissues and absorption of fluid from tissues to blood in the isolated hindlimbs of cats and dogs under conditions such that the arterial perfusion pressure the venous pressure, and the protein osmotic pressure could be independently adjusted to desired constant values.

Capillary pulsation. Capillary pulsation can be recorded only photographically by cinematograph under high power magnification. With low power magnification pulsation in the smaller arteries would be predominant. Visible capillary pulsation is due to vasodilatation or marked aortic regurgitation allowing the arterial pulse to enter the capillaries without adequate damping. The site of the color change is in the subpapillary venous plexus (Lewis, 1927). This capillary or venular pulsation may be general throughout the body or very local.

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CHAPTER 9

ELECTROCARDIOGRAPHY

One of the interesting medical achievements of our time has been the rapid, indeed one might say dramatic, growth of electrocardiography (ἤλεκτρον amber friction of which gives rise to an electrical charge, καρδία, heart, and γράφειν to write) To those of us who received our initial training in this field in the early days of clinical electrocardiography this evolution has been both gratifying and impressive, not to say at times confusing. The confusion has been due to two factors first, the absence at the beginning of an adequate application of fundamental physical laws and principles so that the early growth was more empirical than scientific, and, second, the lack of uniform technic and nomenclature utilized by various workers in the field. This vigorous independence of thought and action has, however its good side, and agreement about utilization of the most satisfactory viewpoints and criteria will naturally follow We are still in the very midst of considerable new research and development in electrocardiography It would be impossible for me in the limited space available in this new edition to expand the chapter sufficiently to present the subject in all of its current detail. I shall retain the story of the evolution of clinical electrocardiography with a brief survey of its present status and refer the reader for a more complete description of technic, debatable theories, and current research to the numerous monographs now available and listed in the Bibliography at the end of the chapter

Electrocardiography is one of the most important methods of cardiovascular examination, ranking in value third after history taking and physical examination. Like cardiovascular roentgenology it has continued to develop rapidly as the result of concentrated study in the past decades.

Near the end of the eighteenth century Galvani and Volta and their followers began their important studies on electricity by utilizing that produced by animals. Galvani, for example, in 1791 used the electrical organ of the torpedo-fish to stimulate not only the muscles and nerves of the frog but also the heart itself.

About the middle of the last century it was learned in the exp

laboratory that when the pigeon's or the frog's heart contracted it produced an electric current (Matteucci, 1843 Kölliker and Müller 1856) For many years after this discovery the heart current of laboratory animals was studied with the crude apparatus at that time available.

Matteucci, Ch. "Sur le courant électrique des muscles des animaux vivants ou récemment tués. *Comptes Rendus des Séances de l'Académie des Sciences*, 1843 XVI, 197

1 The signs of the electrical current of the frog itself, demonstrated by the galvanometer increase in the same instrument in the act of contraction.

"2. *The muscular electrical current* which I shall hereafter call the muscular current, is present in all muscle masses, whatever the animal.

"I have taken pectoral muscles of pigeons, a rabbit's back muscles, hearts of pigeons. In all cases I have obtained a current which flows from the interior of the muscle to the surface. (Translation by myself)

Kölliker A., and Müller H. "Nachweis der negativen Schwankung des Muskelstroms am natürlich sich contrahirenden Muskel. *Verhandlungen der physicalisch-medizinischen Gesellschaft in Würzburg* 1856, VI, 528

"The results which up to now we have obtained from the frog's heart are as follows

1 The apex of the whole heart is electrically negative to any point on the anterior or posterior surface of the ventricles.

"2. Similarly negative is the apex of the heart to the cut surfaces left after removing the auricles without injury to the ventricles.

3 On the other hand the cardiac apex is positive to any cross-section which involves the ventricular musculature itself.

4 Every point on the surface of the heart is positive to any selected cross-section of the ventricle.

"5 The excursion given by connecting the outer surfaces of the base and of the apex of the heart is less than that given by connecting the cross-section of the apex and the surface. (Translation by myself.)

Then came the discovery six decades ago also in the physiologic laboratory that the human heart current could be demonstrated by connecting the outside of the body by electrodes with the capillary electrometer (Waller 1887)

Waller A. D A Demonstration on Man of Electromotive Changes Accompanying the Heart's Beat. *J Physiol.* 1887 VIII, 229

"If a pair of electrodes (zinc covered by chamois leather and moistened with brine) are strapped to the front and back of the chest, and connected with a Lippmann's capillary electrometer the mercury in the latter will be seen to move slightly but sharply at each beat of the heart. If the movements of the column of mercury are photographed on a travelling plate simultaneously with those of an ordinary cardiographic lever a record is obtained as under (fig. 1) in which the upper line h.h. indicates the heart's movements d the lower line l.l. the level of the mercury in the capillary Each beat of the heart is seen to be accompanied by an electrical variation. [This very first published electrocardiogram is essentially

the chest lead reintroduced as Lead 4 into clinical electrocardiography in recent years.]

"The first and chief point to determine is whether or no the electrical variation is physiological, and not due to mechanical alteration of contact between the electrodes and the chest wall caused by the heart's impulse. To ascertain this point accurate time measurements are necessary a physiological variation should precede the movement of the heart, while this could not be the case if the variation were due to altered contact. Fig. 2 is an instance of such time measurements taken at as high a speed of the travelling surface as may be used without rendering the initial points of the curves too indeterminate. It shows that the electrical phenomenon begins a little before the cardiographic lever begins to rise.

"That a true electrical variation of the human heart is demonstrable, may further be proved beyond do bt by leading off from the body otherwise than from the chest wall. If the two hands or one hand and one foot be plunged into two dishes of salt solution connected with the two sides of the electrometer the column of mercury will be seen to move at each beat of the heart, though less than when the electrodes are strapped to the chest. The hand and foot act in this case as leading off electrodes from the heart, and by taking simultaneous records of these movements of the mercury and of the movements of the heart it is seen that the former correspond with the latter slightly preceding them and not succeeding them, as would be the case if they depended upon pulsation in the hand or foot. This is unquestionable proof that the variation is physiological, for there is here no possibility of altered contact at the chest wall, and any mechanical alteration by arterial pulsation could only produce an effect 0 15 to 0..0" after the cardiac impulse. A similar result is obtained if an electrode be placed in the mouth while one of the extremities serves as the other leading off electrode. The electrical variation precedes the heart s beat as in the other cases mentioned.

The mercury column moved up and down several times with each heartbeat but the records obtained by photographing its shadow were inaccurate because of the inertia of the instrument. Laboriously the electric heart tracings or electrocardiograms were obtained and corrected, and considerable progress in their analysis was made by physiologists at the end of the last century (Bayliss and Starling, 1892) and at the beginning of the present century Finally in 1903 came the announcement of the invention of the accurate and practicable string galvanometer (Einthoven) a few years later this was introduced into hospitals and clinical electrocardiography began.

Einthoven, W "Die galvanometrische Registrirung des menschlichen Elektrokardiogramms, zugleich eine Beurtheilung der Anwendung des Capillar Elektrometers in der Physiologie. *Pflüger's Arch. f d. ges. Physiol.*, 1903 XCIX, 472.

(Page 474) "I have tried to find way to avoid as far as possible the construction of a new curve [that is, a corrected curve, such as it was necessary to construct in the use of the capillary electrometer] in so doing I have at length devised an instrument which satisfies many requirements and is especially suitable to inscribe the human electrocardiogram directly in almost its exact proportions.

"The essential part of this instrument—the string galvanometer—is a thin silver coated quartz fibre, which is stretched like string in strong magnetic field. If

an electric current is led through this quartz fibre the fibre shows a movement which can be observed and photographed by means of considerable magnification, just as is the case with the movement of the mercury in the capillary electrometer. It is possible to regulate the sensitivity of the galvanometer very accurately within wide bounds by tightening and loosening the string. (Translation by myself.)

During the past three decades with the development of audion tube amplification the dead beat mirror galvanometer has been adapted to clinical electrocardiography and is the basis for much of the easily portable apparatus that can be carried to the sickroom for cardiac registration of patients at home in bed The cathode ray has also been utilized to record the electrical activity and sounds of the heart in man, but it is unnecessarily expensive in cost and in the use of high operating voltage for the needs of clinical electrocardiography and phonocardiography although in current research it is being utilized with extensive chest leads to explore details of the course of electrical discharge and repolarization through the heart muscle (Goldman)

A recent innovation has been the utilization of an ingenious device of a heated stylus which, activated by a galvanometer moves without friction or overshooting over the surface of a moving processed (wax-covered) paper strip to inscribe the electrocardiogram directly without the trouble, time, and expense of photographic technic. This type of direct writing electrocardiograph has the advantage of accuracy in recording over the initial ink-writing galvanometers which were originally introduced to simplify the clinical technic

At first electrocardiography was sought and used chiefly as an aid in the explanation of cardiac arrhythmia, tachycardia, and bradycardia, having proved to be more satisfactory than the mechanical graphic methods previously employed because of the greater ease of technic and interpretation and because of the more complete information afforded. As time went on, however it was learned that more important data about the heart than the explanation of abnormalities of rate and rhythm are shown by the electrocardiogram from a study of the shape, direction, amplitude, and time relations of the individual waves or deflections, especially as they are compared in various leads.

It is unfortunate that we do not even as yet know the range of the normal electrocardiogram It is wider than we thought it was ten years ago, and much service can still be wrought by the simple electrocardiographic analysis of many thousands of normal individuals. It is also important to become familiar with the electrocardiogram in infancy which is different from that in older children and adults not only in much faster heart rate but in much narrower time intervals, especially *P R* interval and *QRS* duration (shorter by one third to one half—see Figure 54 page 214) and in its normal right axis deviation. It is interesting that the human infant's type of electrocardiogram becomes recognizable at the end of the first month of fetal life (Marcel and

Recently cathode ray electrocardiography by radio (remote control) has been introduced by Holter of Helena, Montana (1949) and by Kanetsoulis of Athens, Greece (1950)

Exchaquet, 1938) also exploration of the maternal abdomen to obtain fetal electrocardiograms has been found successful in 85 to 90 per cent of cases (Goodyear et al. 1942)

The electrocardiograph does not take the place of such other methods of examination as history taking percussion auscultation and roentgenology but it does obviate in large part the need of taking mechanical graphic records of arterial and venous pulses and of the apex impulse. *Finally it must be realized that the electrocardiogram may be perfectly normal even in the presence of serious heart disease* This method of study should therefore be viewed modestly as helpful but not accorded too great importance

The electrocardiogram itself is written by the spread of electrical activity that sweeps down the heart from its pacemaker at each heartbeat, in peristaltic waves over the atria and by special conduction tracts and fibers into the ventricles (Figure 39)

It is the movement of the string shadow or beam of light that causes the waves (usually called deflections or complexes) of the electrocardiogram.

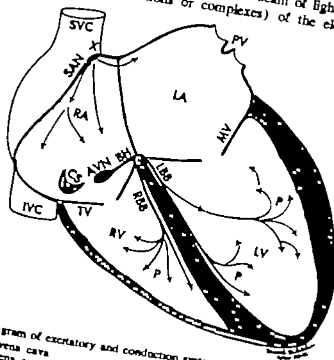


FIG. 39 Diagram of excitatory and conduction system of the heart.

SVC, superior vena cava
IVC, inferior vena cava
RA, right atrium
CS, coronary sinus
TV tricuspid valve
RV right ventricle
PV pulmonary veins
LA, left atrium
MV mitral valve
LV left ventricle
SAN sinoatrial node
X, usual site of pacemaker
AVN atrioventricular node
BH bundle of His
RBB, right bundle branch
LBB, left bundle branch
P Purkinje network radiating out from papillary muscles

(Graybiel and White *Electrocardiography in Practice* W B. Saunders C Philadelphia.)

These waves, chiefly three have been variously named The German school at first labeled them *a* for atrial wave, *i* for the first or initial ventricular wave, and *f* for the second or final ventricular wave these designations have been justified by time but they have not been generally adopted. Einthoven's letters, arbitrarily taken from the middle of the alphabet and attached to the deflections so as not to prejudice future workers in the study of the cardiac mechanism, have become universally employed and will be used here the first deflection, or atrial wave, is called *P* the second deflection, or the first ventricular wave, a rapid succession of one, two or three deflections, is called *Q* *R* and *S* and the third deflection or second ventricular wave, is called *T* (Figure 40) There is often a small final and unexplained wave called *U*

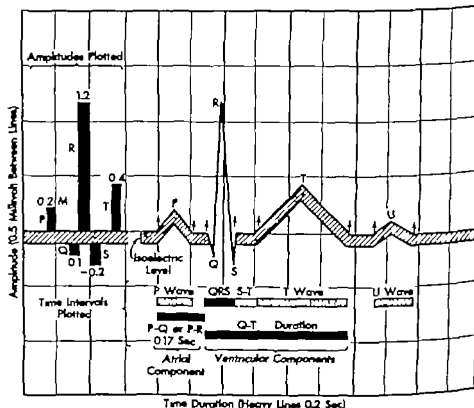


FIG. 40. Diagram of normal electrocardiogram showing the individual complexes with special reference to amplitude and time duration. P = atrial deflection; QRS = first ventricular deflection ST segment and T wave = remainder of ventricular activity beginning of Q to end of T = duration of systole.

There are two essential methods of description of the normal and abnormal electrocardiogram (1) that of the detailed analysis of the individual complexes or waves, which will be largely covered in the present chapter and (2) that of the presentation of the characteristics of the records as a whole, that is, of the patterns which will be presented largely in other chapters, for

example, the electrocardiographic patterns of certain congenital defects, of *mitral stenosis, of the hypertensive heart and the cor pulmonale*, of pericarditis, and of myocardial infarction.

ELECTROCARDIOGRAPHIC LEADS

The first and fundamental step in studying electrocardiograms is to become familiar with the so-called electrocardiographic leads. An electrocardiographic lead" is the connection of any two parts of the body by electrodes and wires with the recording galvanometer Although two electrodes may be attached to any parts of the body (if they are not both too far from the heart or too close together) to lead the heart current to the galvanometer it has become customary for convenience and other reasons to make use clinically of the forearms, the left leg, and the precordium. An esophageal lead point to explore the left atrium and base and posterior portion of the left ventricle has been proposed and tried with results of some interest, but the procedure is not clinically practicable

Direct leads from various points on the heart surface itself present the most detailed information possible concerning the spread of the excitation wave, and aberrations thereof to the individual heart chambers and their anterior posterior and lateral walls. The best substitute for such direct leads in man has been found to be precordial leads with exploring electrode placed on the skin as directly as possible over the part of the heart which it is desired to study Thus many thoracic lead points are possible in the various intercostal spaces and around the chest, and even in the esophagus. We have not yet nearly enough information to be sure of the most desirable positions, and indeed they are already known to vary from person to person according to the body build and the position and type of heart disease, but certain points have already been selected and made the object of considerable study in normal and abnormal subjects more about these below An important consideration in obtaining these precordial, or close up, leads is that the other or as it is sometimes called, indifferent, remote, or peripheral electrode should be placed far from the heart itself on one of the extremities or on the back or by an ingenious arrangement introduced by Wilson to neutralize the effect of any one extremity by connecting all four extremities to a central terminal as the remote electrode point. The concentration of interest on the precordial leads initiated what has been called essentially a unipolar lead.

Quickly following suit unipolar limb leads have been introduced to join the unipolar and bipolar chest leads they were at first in major part elaborated by Goldberger (1947) In the early days of these so-called "unipolar" limb leads it was thought that they had a rather mysterious superiority over the old classical "bipolar" limb leads, particularly in revealing more accurately the electrical (and also often the anatomic) position of the heart and otherwise obscure myocardial disease but more recently it has been shown by Gr and others that they actually merely supplement the bipolar limb

allow us to establish with greater accuracy the projection of the axis and abnormalities thereof on the frontal plane of the thorax, thus expanding Einthoven's triangle (see below) into a figure with six axes, the three of the unipolar leads being perpendicular to the three of the bipolar leads so that there is only a 60 degree instead of a 120 degree interval between the axes (as will be illustrated later in the chapter)

Although the very first published electrocardiogram (Waller *1887*) was a chest lead, convenience and chance led early electrocardiographers away from the thorax itself to limb connections, and only in late years has there been a return to the precordium as an important focus of attention. The precordial leads at this writing (1950) appear to have a double value as compared with the limb leads they reveal the electrical axis projection on the anteroposterior (more or less sagittal) plane at right angles to the frontal plane, thus completing the resultant projection of the direction and magnitude of the electrical axis in space, but also because of their close proximity to the heart itself they show more clearly myocardial abnormalities closest to them. Nevertheless it is not likely that the limb leads as now taken will be abandoned soon inasmuch as they readily reveal normal variations and abnormalities *in the frontal plane. The heart is a solid body and so should* be explored electrically from all directions. Eventually technics such as those developed by Duchosal and by Goldman (see below) or something newer still may replace the present procedures but as yet they have not been developed for practical routine use.

In summary the reasons for taking these three types of leads are as follows. We continue to register the *bipolar limb leads* because we are familiar *with them after many years of use*, because they clearly *suffice to demonstrate* the mechanisms responsible for tachycardia, bradycardia, and arrhythmia, because they are important in helping to establish the projection of the electrical axis and abnormalities thereof in the frontal plane, and because they have become in many instances a part of the useful electrocardiographic patterns with which we have become familiar during the past decade, such as those of the acute cor pulmonale, congenital atrial septal defect, and advanced mitral stenosis (or chronic constrictive pericarditis involving preponderantly the left heart chambers) The *unipolar limb leads* are registered because they are especially helpful in demonstrating the position of the heart with or without complications of heart disease itself thus the right arm lead always (except in cases with dextrocardia) faces the interior of the heart and so normally all its complexes are inverted the left arm faces the outside wall of the heart when the heart lies horizontally or diagonally with resultant upright complexes, and the inside of the heart (as does the right arm lead) when the heart is vertical, giving inverted *QRS* and *T* waves; the left leg lead never faces the inside of the heart although it is at right angles to its axis when it lies horizontally thus yielding under such conditions small, almost isoelectric, complexes. The *unipolar precordial leads* are registered because of their double value just discussed in the preceding paragraph.

Thus ordinarily now the three bipolar and the three unipolar limb leads,

nd several (preferably six) precordial leads are registered for each patient tudied, these leads have been called Leads 1 2, 3 aVR, aVL, aVF and recordial or Chest Leads 1 to 6 or more respectively (Figure 41) In routine terpretation at the present time (1951) it is convenient to analyze first the recordial leads since they often give the most information.

BIPOLAR ("CLASSICAL) LIMB LEADS

Lead 1 consists of the connection of the right lower arm to one end of the alvanometer string and of the left lower arm to the other end, so that the reponderant spread of the action current (which has been called the wave

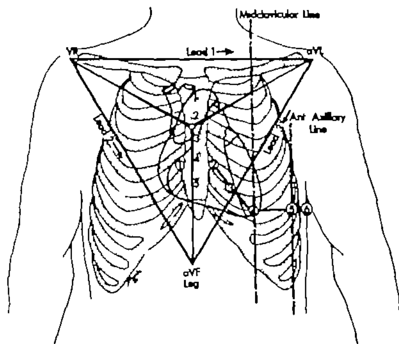


FIG 41 Diagram showing bipolar limb leads (1, 2, 3) unipolar limb leads (VR, VL, VF) and precordial leads (V to V inclusive) The outline of the heart is shown under the *sternum and ribs*, the level of the first five interspaces is indicated. Einthoven triangle is represented, as is also the spatial relationship of the emote electrode to the limb electrodes in the case of the unipolar limb leads.

of relative negativity) in the direction of the lead, that is, from right arm to left, is represented normally in the electrocardiogram by an upright deflection of the string shadow while its reverse direction is represented by an inverted deflection.

Lead 2 consists of a similar arrangement, but with electrodes on right arm and left leg. Either leg may be used with little or no change in the records obtained, since both legs show almost the same difference of electric potential

allow us to establish with greater accuracy the projection of the axis and abnormalities thereof on the frontal plane of the thorax, thus expanding Einthoven's triangle (see below) into a figure with six axes, the three of the unipolar leads being perpendicular to the three of the bipolar leads so that there is only a 60 degree instead of a 120 degree interval between the axes (as will be illustrated later in the chapter)

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In summary the reasons for taking these three types of leads are as follows. We continue to register the *bipolar limb leads* because we are familiar with them after many years of use, because they clearly suffice to demonstrate the mechanisms responsible for tachycardia, bradycardia, and arrhythmia, because they are important in helping to establish the projection of the electrical axis and abnormalities thereof in the frontal plane, and because they have become in many instances a part of the useful electrocardiographic patterns with which we have become familiar during the past decade, such as those of the acute cor pulmonale, congenital atrial septal defect, and advanced mitral stenosis (or chronic constrictive pericarditis involving preponderantly the left heart chambers) The *unipolar limb leads* are registered because they are especially helpful in demonstrating the position of the heart with or without complications of heart disease itself thus the right arm lead always (except in cases with dextrocardia) faces the interior of the heart and so normally all its complexes are inverted, the left arm faces the outside wall of the heart when the heart lies horizontally or diagonally with resultant upright complexes, and the inside of the heart (as does the right arm lead) when the heart is vertical, giving inverted *QRS* and *T* waves; the left leg lead never faces the inside of the heart although it is at right angles to its axis when it lies horizontally thus yielding under such conditions small, almost isoelectric, complexes. The *unipolar precordial leads* are registered because of their double value just discussed in the preceding paragraph.

Thus, ordinarily now the three bipolar and the three unipolar limb leads,

ossible over the cardiac apex. However it rather quickly became apparent at even with care it was not always possible so to place it, that even though were so placed it would usually emphasize normality or abnormalities of at a localized area of the heart wall, and that it might be so close to the entricular sulcus or so perpendicular to the spatial axis of the heart that a light displacement to either side would shift its position from one ventricle to the other or from negative to positive side of the anteroposterior plane of the thorax (or vice versa) with a great change in the pattern. Therefore, an isolated *Lead 4* was given up by most workers in the field a few years ago.

It was also stated in the last edition of this book that multiple precordial (chest) leads should be taken in special or doubtful cases and that the author and his colleagues were taking three such leads (CF_2, CF_4 and CF_6) when necessary rarely more at that time. Our own experience and that of many others soon caused us to take three precordial leads routinely with the exploring electrode at points 2, 4 and 5 and as time went on over 2, 4 and 6 instead and with Wilson's central terminal (V) for the indifferent lead point instead of the left leg (as had been our choice) or the right arm (as was often the choice of others). Finally with more experience in the course of time we began to take all six precordial V leads in addition to the six limb leads mentioned above, so that for the sake of the valuable extra information afforded we now take 12 routine leads instead of the 3 that we took at the time of the first edition of this book (1931), the 4 that we frequently took at the time of the second edition of the book (1937) and the 6 that was our custom at the time of the third edition of the book (1944). In fact on occasion we may now explore further still, as in the case of a special atrial lead (high up over the right atrium) or of a lead (sometimes called 7) on the back at the left posterior axillary line. It is still too early to know how far we had best explore and just what technics we shall eventually use.

Multiple precordial leads (Figure 41) have become standardized as follows, the prefix depending on the position of the indifferent electrode or lead point—CR (chest—right arm), CL (chest—left arm), CF (chest—left leg) and CV usually abbreviated now to V

1 or CR_1, CL_1, CF_1, CV or V_1—the exploring electrode at the *right* border of the sternum in the fourth intercostal space.

2 or CR, CL_2, CF_2, CV_2, or V_2—the exploring electrode at the *left* border of the sternum in the fourth intercostal space

3 or CR_3, CL_3, CF_3, CV_3, or V_3—the exploring electrode midway on the line joining 2 and 4

4 or CR_4, CL_4, CF_4, CV_4, or V_4—the exploring electrode at the left midclavicular line in the fifth intercostal space. We used to try to place this electrode at the cardiac apex, but the variability of the position of the latter both in health and in disease, rendered that location very unreliable and unsatisfactory

5 or CR_5, CL_5, CF_5, CV_5, or V_5—the exploring electrode at the anterior

during the cardiac cycle the left leg is, however the customary lower point.

Lead 3 consists of the connection of the galvanometer with left arm left leg, in comparison with Lead 2, the left leg lead continues to be the l contact, while the left arm is substituted for the right arm.

Thus these three lead points, right arm left arm and left leg, when c nected, form a triangle, which is essentially equilateral. Electrically and g metrically Lead 2 is equal to the sum of Leads 1 and 3 since the differ of electric potential between right arm and left leg is the same whether connect the lead points directly or in a roundabout way Therefore the P_2 should equal P_1 plus P_3, QRS_2 should equal QRS_1 plus QRS_3, and T_2 shou equal T_1 plus T (these letters refer to atrial and ventricular deflections in th electrocardiogram soon to be discussed, while the appended numbers refer t the particular leads—1 2 and 3) Similarly Lead 2 minus Lead 1 equal Lead 3 and Lead 2 minus Lead 3 equals Lead 1 This fact, although useful clinically in checking the accuracy of standardization of the various lead is often ignored.

UNIPOLAR LIMB LEADS

Lead aVR is the new customary so-called augmented (a) that is amplifie 50 per cent, unipolar (V a symbol) right arm (R) lead. The exploring elec trode is attached to the right arm and connected to one pole of the galvanom eter while the other pole is connected to the indifferent lead point which l the case of the unipolar limb leads has been found to serve best when attache to the three limbs not being explored. V is a designation introduced by John ston—personal communication, 1951—to indicate leads taken with a centr terminal and derived from its usage by electrical engineers and physicists as a symbol of electrical potential It was not originally intended as an abbreviation for vector

Lead aVL is the augmented unipolar left arm lead, with exploring electrode on the left arm and indifferent lead point connected to the right arm and both legs.

Lead aVF is the augmented unipolar left leg (F for foot) lead with ex ploring electrode on the left leg and indifferent lead point connected to both arms and right leg.

It is important and convenient to know that, when added together the three unipolar limb leads, aVR, aVL, and aVF equal zero.

PRECORDIAL (CHEST OR THORACIC) LEADS

In the last (third) edition of this book much was said about *Lead 4* which had been called the "standard" or indeed even the classical" chest lead It had been taken by attempting to place the exploring electrode as near as

ghth and ninth leads over the left back, and right anterior chest leads, numered from midline to the right, like the precordial leads and, as advised y Kisch, with the first lead point at the midsternum (level of fourth inter pace) for both sides

It is obvious that the "unipolar" chest leads, taken as Wilson has recom ended (CV) leads, give a more accurate appraisal of the potential at the arious precordial lead points than do the bipolar leads, although there is by o means so great a difference as in the case of the unipolar and bipolar

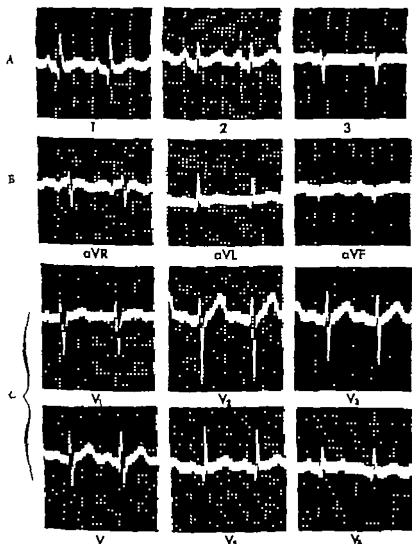


FIG. 43 Electrocardiogram of normal individual of heavy build with horizontal heart position. (A) Bipolar limb leads 1 2, and 3 (B) unipolar limb leads, VR, VL, and aVF (C) six precordial leads, V to V inclusive. Time = 0.04 and 0 20 second, amplitude 1 mm = 0.10 m

limb leads. This is, of course, due to the fact that the greater the differe in distance of two electrodes from the heart the less the error due to potential of the point to which the indifferent electrode is attached. The bipolar chest leads, described above, approach in accuracy the "unipol chest leads of Wilson. For this reason and especially for the sake of more uniformity it is suggested that for routine use the V leads be now employed has been my own recent custom.

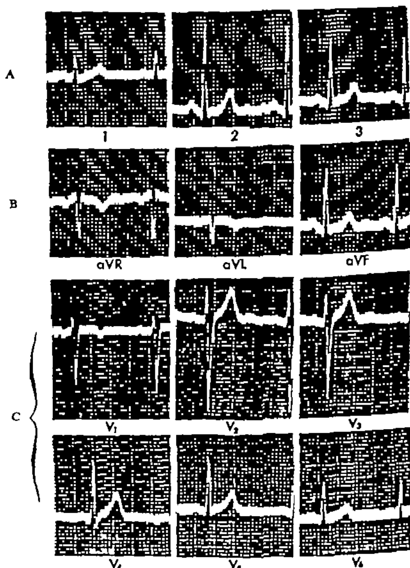


FIG. 44 Electrocardiogram of normal tall individual with vertical heart positi (*A*) Bipolar limb leads 1, 2, and 3 (*B*) unipolar limb leads, VR, VL, and V (*C*) unipolar precordial leads V to V inclusive. Time = 0.04 and 0.20 second, amplitu mm = 0.10 m

Intracardiac and esophageal leads have been used in research and for study of very special cases the former during catheterization of the right atrium and right ventricle and the latter for exploration of the left atrium and posterior wall of the left ventricle. They serve as unipolar leads to explore these particular parts of the heart and although, during acute myocardial infarction, it is not wise to subject the patient to esophageal electrocardiography it is possible in chronic cases to identify a posterior myocardial scar and also to uncover atrial action not apparent in other leads. The right intra-atrial electrocardiogram shows normally an inverted *P* wave high in the atrium in the vicinity of the s-a node, an upright *P* wave low in the atrium, and a diphasic *P* wave in intermediate positions while the ventricular complex varies from a *QS* to a *QR* most commonly or even less often (near the ventricle) to a *RS* all with negative *T* waves. The right intraventricular electrocardiogram shows normally an upright *P* wave and an *RS* with a negative *T* Esophageal leads show a slightly later *P* wave over the left atrium by about 0 05 second than the *P* wave recorded by the right intra atrial electrode.

In the esophageal lead the *P* wave is, as a rule, unusually prominent and high and the *QRS* and *T* waves are normally inverted unless the polarity is reversed in which case an inverted *T* wave is indicative of disease (usually infarction) of the posterior wall of the left ventricle.

CARDIAC VECTOR AND ELECTRIC AXIS

A vector is a force which has direction and magnitude and electrically either a negative or a positive charge. In electrocardiography it has been loosely called the electrical axis of the heart. Fundamentally electrocardiography is the analysis of the cardiac electrical vectors and there are various technics for their demonstration, all of which are more or less crude and in the process of further development, including the old classical bipolar limb leads with the much debated, but still scientifically applicable, Einthoven triangle, the unipolar limb leads, the precordial leads, and the more basic but least developed technic of all, namely that of vectorcardiography

When the excitation wave spreads from normal or abnormal pacemaker through the heart, it is attended by a wave of electric activity which takes a complicated manifold path (see Figure 39 page 183) The diffuse course can be represented by the *QRS* loop a curve not lying in a single plane but in space as does the heart itself A further reduction of this curve has hitherto been necessary to suit the limited boundaries of electrocardiography and so we can determine its projection on the anterior plane of the body to fit into the triangle of the three classical leads or on any other plane, for example, specifically sagittal or horizontal. Finally for further convenience the curve is simplified by constructing its resultant, a straight line to show the consequent angle and magnitude This resultant of the projection of the true axis of the distributed electric potential of the heartbeat is what we briefly designate as the electric axis of the electrocardiogram. It can be determined by calculation

from any two of the three classical limb leads by formula or by diagram, using what is called Einthoven's triangle. It has been of some clinical interest and value to make this calculation in cases showing an abnormal deviation of the angle (the normal range of angle is from −20° to +100°, but usually +20° to +70°). The formula is as follows: *tangent of alpha* $= \frac{2e_2 - e_1}{e_1\sqrt{3}}$, when alpha equals the angle between the axis and the horizontal, e_2 the amplitude in millimeters of the *QRS* wave in Lead 2, and e_1 that of the *QRS* in Lead 1. The length of the axis, or the manifest potential difference (E), is calculated from the following formula: $E = \frac{e_2}{\cos(\alpha - 60°)}$. More convenient than these formulas has been the employment of the diagram of the triangle of the leads (Figure 45, Einthoven's triangle). Leads 1 and 3 are usually employed in this calculation. The amplitude of $R_1 - S_1$ is plotted on the Lead 1 line, and that of $R_3 - S_3$ on the Lead 3 line; perpendiculars are dropped from these points to their points of intersection. Lines are then drawn out from the center of the circle through these points of intersection to the circumference of the circle; the angles with the horizontal diameter of the circle, the zero line, are read off, the degrees being noted as positive around the semicircle clockwise to 180°, and as negative counterclockwise. This is a crude but clinically convenient and useful method. It affords only a very general measurement and shows no detail of the axis deviation. If at the present time, however, greater detail and accuracy are attempted the method becomes complicated and difficult. Although it is of some academic interest to know not only the resultant axis deviation but its whole curve, that is, the individual deviations at various phases, it is of much greater interest to know the direction of the curve in space, for example, how much of it is bent backward in the anteroposterior plane, a feature not shown at all in the frontal plane. It is to be noted that to secure adequate information accurately for even one (e.g., the frontal) plane two electrocardiographic leads must be registered simultaneously to make sure of the synchronicity of phases; for example, the top of the *QRS* peak in Lead 1 is often not synchronous with either peak (or nadir) of downstroke in Lead 3. A further development of the representation and analysis of the cardiac vector (electric axis) in space has been the construction of the vectorcardiogram both by projection on the three planes and by tridimensional models (see below).

The direction of the resultant electric axis of the heart in the frontal plane lies within wider limits than does the anatomic axis, both normally and abnormally. The normal electric axis lies between the degrees −20 and +100 of Einthoven's triangle (Figure 45). If the angle is more minus than −20°, that is, much above the horizontal, there is so-called abnormal left axis deviation, and if it is beyond +100°, that is, considerably to the right of the vertical, there is abnormal right axis deviation.

The term "abnormal left and right axis deviation" as applied to the classical bipolar limb leads does not have the same significance as "left and right

ventricular preponderance." *Displacement of the heart upward* by a high diaphragm so that the heart lies horizontally will give abnormal left axis deviation even though the left ventricle remains normal, while a low diaphragm with vertical heart position will tend to give abnormal right axis deviation even though the right ventricle is small and the left ventricle actually preponderant. It is true however that when we find high degrees of abnormal

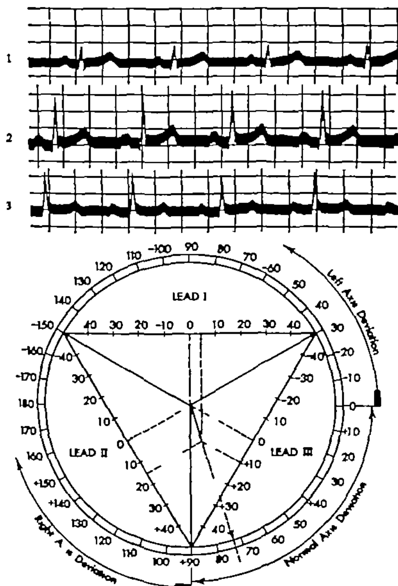


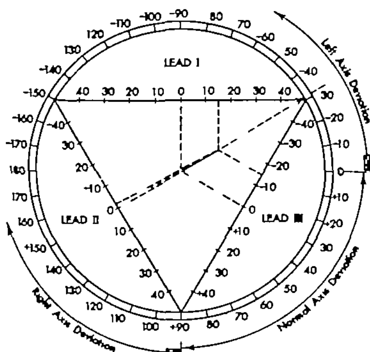
FIG. 45. Electrocardiogram (Leads 1 2, and 3) and Einthoven triangle showing normal angle of the electrical axis.

from any two of the three classical limb leads by formula or by diagram, using what is called Einthoven's triangle. It has been of some clinical interest and value to make this calculation in cases showing an abnormal deviation of the angle (the normal range of angle is from −20° to +100°, but usually +20° to +70°). The formula is as follows: *tangent of alpha* $= \frac{2e_2 - e_1}{e_1\sqrt{3}}$, where alpha equals the angle between the axis and the horizontal, e_2 the amplitude in millimeters of the *QRS* wave in Lead 2, and e_1 that of the *QRS* in Lead 1. The length of the axis, or the manifest potential difference (E), is calculated from the following formula: $E = \frac{e_2}{\cos(\alpha - 60°)}$. More convenient than these formulas has been the employment of the diagram of the triangle of the leads (Figure 45, Einthoven's triangle). Leads 1 and 3 are usually employed in this calculation. The amplitude of $R_1 - S_1$ is plotted on the Lead 1 line, and that of $R_3 - S_3$ on the Lead 3 line; perpendiculars are dropped from these points to their points of intersection. Lines are then drawn out from the center of the circle through these points of intersection to the circumference of the circle; the angles with the horizontal diameter of the circle, the zero line, are read off, the degrees being noted as positive around the semicircle clockwise to 180° and as negative counterclockwise. This is a crude but clinically convenient and useful method. It affords only a very general measurement and shows no detail of the axis deviation. If at the present time, however, greater detail and accuracy are attempted the method becomes complicated and difficult. Although it is of some academic interest to know not only the resultant axis deviation but its whole curve, that is, the individual deviations at various phases, it is of much greater interest to know the direction of the curve in space, for example, how much of it is bent backward in the anteroposterior plane, a feature not shown at all in the frontal plane. It is to be noted that to secure adequate information accurately for even one (e.g., the frontal) plane two electrocardiographic leads must be registered simultaneously to make sure of the synchronicity of phases; for example, the top of the *QRS* peak in Lead 1 is often not synchronous with either peak (or nadir) of downstroke in Lead 3. A further development of the representation and analysis of the cardiac vector (electric axis) in space has been the construction of the vectorcardiogram both by projection on the three planes and by tridimensional models (see below).

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ig 46. Electrocardiogram and Einthoven triangle showing left axis deviation.

average normal angle to an abnormal one (Figure 4 page 43) This influence of displacement may even give abnormal left axis deviation of great degree, *although it often but exaggerates the effect of other factors. An interesting* variation of this type consists of complete negativity of Lead 3 all the complexes—*P QRS* and *T*—being inverted this phenomenon is often found in short, fat individuals with high diaphragms.

2 *Preponderant enlargement of the left ventricle is a common cause* or accompaniment of left axis deviation of high degree Chronic hypertension and chronic aortic regurgitation or stenosis are the most important of the known clinical conditions behind it (see Figure 97 page 477 and Chapter 26)

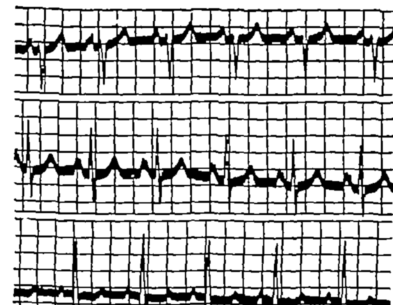
3 *Left bundle branch block (see Chapter 34)* The electrocardiogram of marked left bundle branch block has abnormally wide *QRS* waves, over 0 1 second in duration with moderate amplitude above the baseline in Lead 1 and below the baseline in Lead 3 with rather low voltage or diphasic *QRS* waves in Lead 2 (see Figure 165 page 947) and broad, notched, downwardly directed *QRS* waves over the right ventricle and bifid or slurred *R* waves over the left in the multiple precordial leads. Until fifteen years ago this type of electrocardiogram was thought to indicate right bundle branch block, but convincing evidence from the precordial leads (with late arrival of the intrinsic deflection over the left ventricle) exposed the error of the earlier interpretation.

4 Right ventricular premature beats (see Chapter 32) Isolated instances of abnormal axis deviation occur in the form of ventricular premature beats arising in the right ventricle or near the cardiac base. The *QRS* waves are deformed much as in left bundle branch block but their amplitude is usually much greater In a well-marked instance of right ventricular premature beat the *QRS* is relatively high, the QRS_3 is deep the QRS_2 is diphasic and often of low voltage, and the precordial *QRS* shows an early intrinsic deflection over the right ventricle Years ago these extrasystoles were thought to arise in the left ventricle.

Abnormal right axis deviation (Figure 47) much less common than abnormal left axis deviation, *results from five factors*

1 A vertical heart position or rotation of the heart on its other axes may give rise to abnormal right axis deviation usually not of great degree, the angle rarely measuring more than +95 In the normal person but sufficient to mask other conditions. It is by far the commonest cause of right axis deviation. Deep inspiration may give temporarily a slightly abnormal right axis deviation when the electrocardiogram in quiet breathing shows a tendency toward it. Displacement of the heart to one side or the other by fluid or by air in the pleura, or by lung retraction or pleural adhesions, affects the position of the heart as a rule in toto along with the mediastinum, without causing any important change in axis deviation, as does also shifting of position from one lateral recumbency to the other as noted above.

2 Preponderant enlargement of the right ventricle with its attendant shift in position *of the heart, particularly by clockwise rotation, is the commonest*



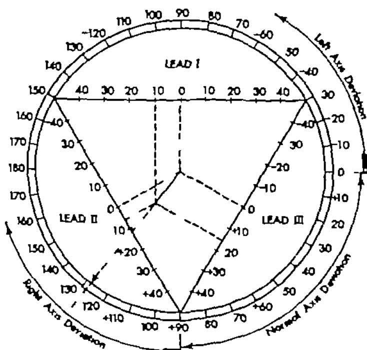


FIG. 47 Electrocardiogram and Einthoven triangle showing abnormal right axis deviation in case of mitral stenosis of high degree.

cause of markedly abnormal right axis deviation, in which there is a sharp moderately deep S_1 with little or no R_1 a diphasic QRS_2 of little voltage, a high R_3 with little or no S_3 and relatively high R waves over the right ventricle and prominent S waves over the left ventricle in the precordial leads. During the first few weeks of life right axis deviation is often present normally in slight degree. After that age moderate or high degrees of right axis deviation are caused by three clinical conditions mitral stenosis, congenital defects, and pulmonary disease. Mitral stenosis is frequently found without abnormal right axis deviation, but when that electrocardiographic sign is present, especially if there is atrial fibrillation and no obvious sign of congenital heart disease, that valve lesion is usually found to be present (Figure 129 page 680) Congenital pulmonic stenosis and interatrial septal defects are rarely if ever found without abnormal right axis deviation by electrocardiogram they cause a higher degree of it than does any other condition (see Figure 73 page 320) Rarely the cause of abnormal right axis deviation is chronic pulmonary disease, in particular silicosis or other cause of extensive fibrosis. Very rarely pulmonary endarteritis may be a factor

3 Right bundle branch block is shown electrocardiographically by abnormally wide QRS complexes directed downward in Lead 1 and upward in Lead 3 or by wide S waves (see Figure 166 page 948) In Lead 2 the QRS wave is diphasic as a rule and of low voltage, and in the multiple precordial leads it is M-shaped over the right side of the heart and shows a prominent R wave and wide S wave over the left. This was formerly called left bundle branch block (see Chapter 34)

4 Left ventricular premature beats are isolated instances of abnormal right axis deviation giving high, wide QRS complexes in Leads 2 and 3 QRS waves often of low voltage, slightly or moderately inverted, in Lead 1 and with wide QRS waves in the precordial leads with earlier intrinsic deflections over the left ventricle. A premature beat arising from the left ventricle, although near the right ventricle, has been shown experimentally to give rise to a QRS complex of left ventricular premature beat type. But ventricular premature beats are often neither of definitely right nor of definitely left ventricular type in the electrocardiogram In such cases they may arise in the septum or junctional tissue.

5 Congenital dextrocardia shows a typical electrocardiogram in about half the cases, that is, where there is transposition with general situs inversus (see Figure 65 page 303) There is a complete inversion of all complexes of Lead 1 and an interchange of the usual Leads 2 and 3 due to the fact that with relation to the heart in such a case the right arm corresponds to the left arm of the person with the heart in normal position, and the left arm to the right. When an electrocardiogram shows a completely inverted Lead 1 it is pathognomonic of congenital dextrocardia provided there is no error in technic namely a crossing of electrode wires. The precordial leads show the usual normal characteristics when the exploring electrode is placed over the right side of the chest.

Vectorcardiography A further and natural evolution of the study of the cardiac vector is its determination and demonstration in space, that is, in three dimensions, and also in time, which is of prime importance too, since the duration as well as the distance, direction, and magnitude of the cardiac vector is significant. Various technics have been introduced to study the vector projected on the frontal plane as already noted, including among others that recently devised by Goldman using the cathode ray oscillograph and many lead points over the entire precordium which result in waves of darkness and light representing *P* *QRS* and *T* waves sweeping over the field.

Also desirable as an eventual goal when it can be routinely introduced is the spatial (and time) recording of the cardiac vector which has been called vectorcardiography Various investigators have studied the problem. Mann was one of the first who did so calling the resulting curve the monocardiogram (1920 and 1938) Duchosal and Sulzer (1949) are also pioneer workers who have developed the method more fully with the actual construction of models of the *P* *QRS* and *T* waves (vectorcardiography) based on the projections of cathode ray oscillograms of the cardiac vector on two planes of a trihedron with the time marked off by beads attached to the wire loops representing the course of the vectors (Figure 48) Figure 49 shows the relationship of the trihedron of Duchosal and Sulzer to Einthoven s triangle and the unipolar chest lead points. Much time will be needed to determine the range of normal vectorcardiograms and abnormal patterns.

My friend and former associate Dr J W Hurst of Atlanta, Georgia, experienced in recent developments in certain technics of the application of vectorcardiography in this country has kindly prepared for me the following insert (personal communication, March, 1951)

"Grant and his co-workers have presented a method for determining the spatial direction of the fundamental electrical forces of the heart by simple inspection of routine electrocardiographic leads. Since this method appears promising, it is mentioned here for completeness. For greater details and proof of the method, the reader is referred to the Bibliography

"To determine the direction of the mean *QRS* *ST* and *T* forces in the frontal plane, the six extremity leads are inspected to determine which lead has the largest deflection and which lead has the smallest deflection. The resultant area of each deflection is used to determine its relative size. The resultant area is determined by adding the positive portions of the curve to the negative portions algebraically The mean vector will be parallel to the lead axis with the largest resultant deflection or perpendicular to the lead axis with the smallest resultant deflection, and its direction must satisfy the polarity of all six extremity leads. With practice one will soon learn to interpolate between the extremes of vector positions just mentioned so that the range of error will be only 5 to 10 degrees. The direction of the instantaneous vectors can be determined in a similar manner by breaking up the *QRS* and *T* deflections into small individual portions. If one remembers that Lead 1 + 3 = 2 and that aVR + aVL + aVF = 0 then the determination of the direction of

the various vectors becomes quite accurate. By the above reasoning one can determine the frontal plane projection of the mean spatial *QRS ST* and *T* vectors and spatial *QRS ST* and *T* loops.

After identifying the direction of the frontal plane projection of a spatial vector one then locates the transitional complex in the precordial leads. (A transitional complex is equally negative and positive or resultantly zero.) The transitional complex is recorded along the transitional pathway on the chest which is "produced" by a plane perpendicular to a spatial vector at its origin extended to the surface of the volume conductor. The location of this plane which is perpendicular to the spatial vector under study will, therefore, deter-

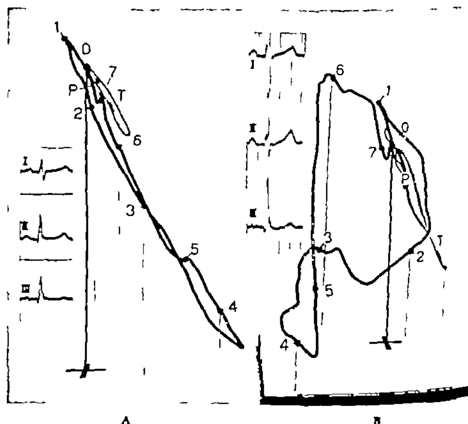


FIG. 48 (*A*) Photograph of wire loop representing the vectorcardiogram of normal individual. The timing of the long, obliquely placed *QRS* loop indicated by heavy black wire, is shown by beads from 0 to 7 (time interval = 0.01 second). The *P* loop is made of thin wire scarcely visible. The *T* loop is grey in color. The point of origin of all three loops, *P*, *QRS* and *T* is zero. A black column supports the model. At the bottom of the stand cross represents the normal axes of the body: the vertical bar the anteroposterior and the horizontal bar the transverse. The electrocardiogram (limb leads I, II, and III) is shown at the left of the loop. (*B*) Wire loop representing the vectorcardiogram of a case of the tetralogy of Fallot with the graphs of the complexes and the electrocardiogram represented as in the case of *A*. (Kindness of Dr. Pierre Duchosal, Geneva, Switzerland.)

mine the anterior or posterior displacement of a vector from the frontal plane thus identifying its spatial position. If the thorax is assumed to be a cylinder which is a reasonable assumption electrically speaking, it is quite easy to visualize the transitional pathway and its relationship to the spatial vector. The method described allows one to determine the mean spatial vectors and by similar reasoning the spatial instantaneous vectors can be visualized. The range of error in determining the spatial direction of electrical forces approaches 15 degrees.

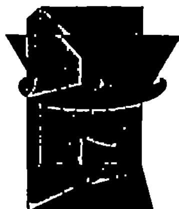


FIG. 49 Drawing in perspective of the plans of derivations according to several systems. The rectangular trihedron symbolizes the derivations of the vector the equilateral triangle that of the limbs, and the ellipse those of the precordium. (Kindness of Duchosal and Sulzer: Figure 43 page 88 of their book, *La Vectocardiographie* S. Karger Bâle and New York, 1949.)

"In a general sort of way the *QRS* vector indicates the direction of the electrical field in the chest, and it becomes totally unnecessary to memorize various deflection contours in order to determine such a position. The spatial *QRS-T* angle is an extremely useful tool. It should be apparent that the *QRS* vector and *T* vector produce the sides of the parallelogram which is necessary to construct the ventricular gradient, and therefore the *QRS-T* angle incorporates certain of the properties of the gradient. The spatial *QRS-T* angle varies with age and in the normal adult is usually less than 60 degrees.

"The electrocardiogram of a patient with a normal heart is shown analyzed by the vectoral method in Figure 50.

"The electrocardiogram of a patient with an extensive anterior myocardial infarction is shown analyzed by the vectoral method in Figure 51."

Electrocardiographic gradient. Closely related to the cardiac vector and the electric axis is the so-called gradient, which may be calculated for either atria or ventricles, although to date attention has naturally been focused, as in other such studies, on the ventricles. The ventricular gradient, as defined by Burch

and Winsor (1949) is a vector expression (in quantitative terms) of the relative variations in duration of the excited state in the different portions of the ventricular musculature Thus $\hat{G}$ (the ventricular gradient as projected on the frontal plane of the body) = the sum of $\hat{A}_{QRS}$ (the mean manifest magnitude of the *QRS* complex determined algebraically and measured in microvolt seconds or units, i.e. the mean force of the depolarization process of the ventricular musculature) plus $\hat{A}_T$ (the mean manifest magnitude of the *T* wave, which represents the repolarization process, in microvolt seconds or units). The caret placed over the symbols indicates a vector value.

The technic of the measurement of the ventricular gradient consists of

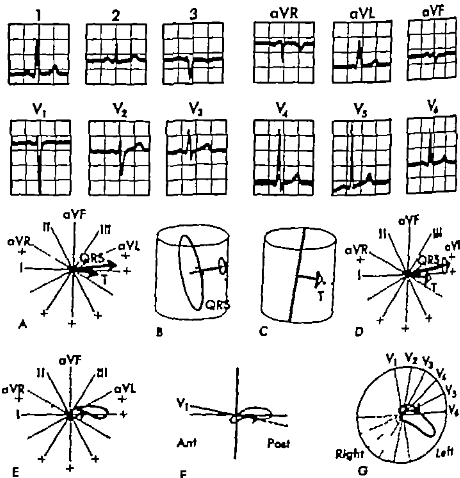


Fig. 50. Thirty-seven-year-old normal male illustrating horizontal position of the mean *QRS* vector (*A*) Mean *QRS* and *T* vectors as seen in the frontal plane (*B*) mean spatial *QRS* vector as seen in a cylindrical volume conductor (*C*) mean spatial *T* vector as seen in a cylindrical volume conductor (*D*) final "summary" figure to illustrate the spatial *QRS* and *T* electrical forces, (*E*) frontal plane *QRS* loop (*F*) sagittal plane *QRS* loop and (*G*) coronal plane *QRS* loop, seen from below (Kindness of Dr L Willis Hurst, Atlanta.)

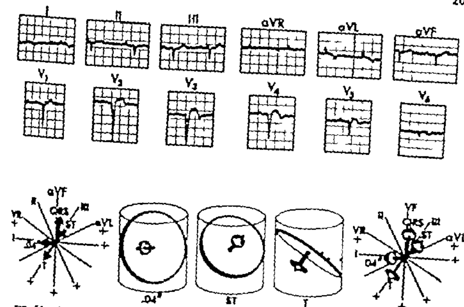


FIG. 51 The electrocardiogram shown above is from 50-year-old male with characteristic history of myocardial infarction. The figure to the left shows a six axial lead arrangement which is produced by superimposing the unipolar extremity lead axes on the tri-axial reference system of Bayley. This figure shows the frontal plane projection of the spatial *QRS* *ST* *T* and .04 vectors. Note that the mean *QRS* is only slightly positive in Lead 1 and is negative in Leads 2 and 3 and also fits the polarity of the unipolar extremity leads. The mean *T* vector is perpendicular to Lead aVR and the force is largest in Lead 3. The mean *ST* vector is slightly negative in Lead VR and the first .04 second of the *QRS* loop is approximately perpendicular to Lead VF. The edge of the circular disc represents the transitional pathway along which transitional complexes will be recorded. The .04 second vector is tilted markedly posteriorly since the initial deflection is negative in Leads V The *ST* vector is tilted markedly anteriorly since the *ST* segment is elevated in all the chest leads. The *T* vector is tilted only slightly anteriorly since the *T* wave is positive in Lead V and negative in Leads V In general, the .04 "dead zone vector" is directed away from an area of myocardial infarction, and the *T* vector is directed away from the ischemic zone surrounding the area of infarction. The *ST* vector is directed toward the area of myocardial injury surrounding the area of infarction. The tracing above represents an extensive anterior myocardial infarction since the .04 vector is directed away from the anterior ventricular wall and the *ST* vector points toward the same area. The *T* vector is directed away from the lateral wall of the left ventricle. The diagram to the right illustrates how the spatial vectors are recorded routinely in clinical practice. (Figure and legend through the kindness of Dr J. Willis Hurst, Atlanta.)

The .04 vector refers to the initial electrical force acting during the first .04 second of the *QRS* loop.

measuring the sum of the areas (A) in microvolt (one-millionth volt) seconds under the *QRS* and *T* waves above the baseline in any two leads (preferably Leads 1 and 3) and subtracting the sum of areas below the baseline (Figure 52A). In the case of a single normal muscle strip (Figure 52B) the gradient would be zero since the depolarization area (R) above the baseline would be neutralized by the repolarization area (T) below the baseline. In human electrocardiography however the situation is very different, there being many

heart muscle masses with varying individual influences per se and as affected by changes in position and rate of the heart as well as by disease. Thus, since in the frontal plane the routine limb leads show normally preponderant upright T waves as well as preponderantly upright QRS waves the normal ventricular gradient in man has been found to average +52 microvolt seconds or 13 0 units (1 unit = 4 microvolt seconds) the range is not certain but has been put at a maximum of 23 0 units and a minimum of about 2.5 units (Burch and Winsor 1949) The gradient of QRS ($\hat{A}_{QRS}$) varies from about +12 0 to about −3 5 units. There is, as yet, little clinical applicability of the ventricular gradient, although primary changes in $\hat{A}_T$ (i.e. not dependent on variations of the QRS wave) may be distinguished by this method.

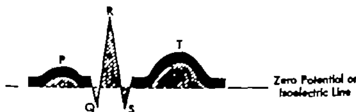


FIG. 52A. Diagram showing the areas subtended by the P and QRS complexes and the area under the T wave. Areas above the isoelectric line are considered to be positive values and those below the isoelectric line are negative.

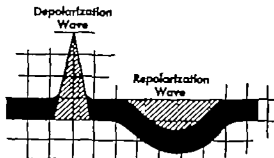


FIG. 52B The process of depolarization and repolarization results in two separate waves which include areas of equal size. (*A Primer of Electrocardiography* 2nd ed 1949 [1st ed., 1945]. Kindness of Drs. George Burch and Travis Winsor and Lea & Febiger Philadelphia.)

ELECTROCARDIOGRAPHIC COMPLEXES AND TIME INTERVALS

THE ATRIAL DEFLECTION OR P WAVE

The normal P wave. Electrical activity of the atria is, as a rule, better defined and studied in Lead 2 than in the other routine leads because the axis of the P (atrial) wave is commonly parallel to Lead 2 for special analysis in difficult cases, however the first precordial lead V_1 may be useful, or best of all a lead with electrode in the third interspace just to the right

of the sternum. Analysis of the normally inverted *P* wave in Lead aVR may also prove helpful.

The P wave of Lead 2 of the electrocardiogram is normally a blunt, rounded, sometimes slightly notched or scalloped upright deflection, 1 to 3 mm high (each millimeter represents in a properly standardized record one tenth of a millivolt) and not over 0.1 second wide at the lower border of the baseline between corresponding points of upstroke and downstroke. This wave represents the spread of excitation over the atria along the muscle bundles from the normal starting point, the pacemaker at the head of the sinoatrial node, which lies at the junction of the superior vena cava and the right atrium (Figure 39 page 183) The atrial electric axis, which is the resultant of the spread of current in all directions over the muscle of right and left atria is normally directed down and to the left in its projection on the anterior plane of the body which is that represented by the routine electrocardiogram. The *P* wave itself is very short in time interval and represents only about one third of the duration of atrial systole it is followed, however by a slight change in baseline of varying extent, usually directed downward, coinciding in time with the rest of the atrial systolic interval, but as a rule concealed by the superimposition of the first ventricular complex or *QRS* wave. In heart block this late evidence of atrial electric activity may sometimes be clearly seen. It has been called the atrial *T* wave or *Ta* deflection (Figure 53)

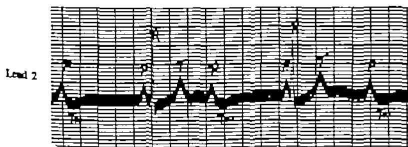


FIG. 53 Electrocardiogram showing *T* waves in complete heart block. Lead

The P wave of Leads 1 and 3 In Lead 1 the *P* wave is called *P* It is of lower amplitude normally than in Lead 2 sometimes it is flat or isoelectric and so may be invisible rarely it may be greater than the *P* wave in Lead 2 (*P*) normally when the *P* wave of Lead 3 (*P*) happens to be inverted. Very rarely the *P* wave may be inverted in Lead 1 when there is normal rhythm such a finding means congenital dextrocardia if an error has not been made in the attachment of the electrodes with resulting totally upside down Lead 1 When *P* is 2 mm or more in amplitude it is abnormal, and the same factors responsible for an abnormally high or wide *P* are also responsible for too large a *P* In other respects, too the discussion about P_2 applies to *P*

In Lead 3 the P wave may normally be upright, isoelectric, diphasic, or even slightly inverted. It is, therefore, the least desirable of the three bipolar limb leads for study of the atrial complex. However arrhythmias may be present in this lead and not in the others and one may also wish to note the character of the P_3 wave to aid in the interpretation of atrial abnormalities in the other leads and of the significance of inversion of T_3.

In the *unipolar limb leads* the *P* wave, like the *QRS* and *T* waves, varies normally in direction and amplitude with the position of the heart. In the right arm lead (aVR) it is almost invariably inverted and often closely resembles, except for its direction, the *P* wave of Lead 2. In the left arm and left leg leads it is upright and of variable height, higher in aVL than in aVF if the heart lies horizontally and vice versa if the heart is vertical.

In the *unipolar precordial leads* V_1 to V_6 inclusive, the *P* wave is not usually so well marked as in the limb leads It may be of fair amplitude, however, and more often upright than otherwise in the first position, just to the right of the sternum, and when the right arm is used as the indifferent or distal lead point in general it may be upright, isoelectric, diphasic, or inverted.

Abnormalities of the *P* wave. The description of the *P* wave abnormalities herein refers in particular to Lead 2 which, as a rule, of the routine leads shows them best.

The *P* wave may show abnormalities of size and shape whether the heart rhythm is regular or not. Moreover the *P* wave itself may remain normal in some instances of irregular or disturbed rhythm, as in heart block. Disorders of rhythm will be considered in the last three chapters of the book. Sinus arrhythmia, however demands a brief discussion now

Due to a variable activity of the pacemaker in the sinoatrial node, caused by vagal influence and often associated with some bradycardia, sinus arrhythmia (Figure 161 page 927) is generally a simple waxing and waning of rate with the intervals between normal *P* waves first decreasing and then increasing in phases related to the corresponding phases of respiration, inspiration and expiration. It is a normal phenomenon most common in children If very marked or not related to respiration it is an abnormal phenomenon, in which case digitalization or faulty coronary circulation or an unknown factor may be responsible The *P* waves may decrease in amplitude with the periods of bradycardia as the pacemaker descends along the sinoatrial node; usually they do not so decrease.

Increase in amplitude (height) of the P wave is usually associated with increase in its width or duration, although one may be present without the other An amplitude of 3 mm or more and a duration, measured between corresponding points of upstroke and downstroke at the baseline, of over 0.1 second are greater than the normal measurements in the subject at rest. Although exercise and sometimes increased sympathetic tone with tachycardia induced otherwise than by exercise tend to increase the height of the *P* wave, even above the usual normal limit, a constant increase in height or width, or both, of the *P* wave is most often found in three conditions, namely mitral

stenosis and two congenital anomalies, atrial septal defects and the tetralogy of Fallot, both of which, especially the first, are associated with considerable atrial enlargement. Hypertension especially with myocardial failure, and, less commonly other ill-defined conditions may cause high *P* waves in the electrocardiogram. When this atrial deflection is abnormally high or wide it tends also to be abnormally notched sometimes the notching is so deep that the deflection appears doubled. Increased width of the *P* wave with or without increase in height is more likely to indicate enlargement of the left atrium, as in mitral stenosis, while preponderant increase in height with or without increase in width is more often found with enlargement of the right atrium, as in the case of a congenital atrial septal defect.

Decrease in amplitude may occur in vagal depression of the sinoatrial node with probable displacement of the pacemaker from the head of the node down toward the tail, and this may be halfway or more along the sulcus terminalis toward the inferior vena cava. This change in *P* wave may be seen to occur gradually or suddenly or it may be a constant finding; it is frequently associated with a slowing of the heart rate. It may sometimes be produced through vagal stimulation by pressure over the carotid sinus, but it also may occur indirectly through the effect of digitalis, or it may infrequently occur spontaneously as, for example, during the slowing of the heart rate at the end of expiration. The clinical condition in which an abnormally low in fact often almost isoelectric or flat, *P* wave is regularly found is hypothyroidism (Figure 92, page 454) due to either myxedema or cretinism. This smallness of the *P* wave in such cases accompanies a tendency to low voltage throughout the electrocardiogram, particularly involving the *T* wave. When the clinical condition improves and the basal metabolic rate rises toward normal under treatment with thyroid gland, the *P* wave also becomes more normal. Under other varied circumstances the *P* wave is occasionally found very low the reasons for which are not clear Heart failure alone does not cause the change.

Absence of the P wave as a separate definite deflection results from several causes. (1) In the first place, this is most commonly due to atrial fibrillation, in which orderly sequence of atrial contraction is replaced by irregular rapid, incoordinated atrial movement (see Chapter 33) (2) In the second place the *P* wave may be replaced by regular instead of irregular baseline oscillations due to another condition closely related to atrial fibrillation, namely atrial flutter (see Chapter 33) (3) In the third place, the *P* wave may be partly or wholly buried in the *QRS* wave or in the *T* wave in cases of atrioventricular block (Figures 53 and 164 page 935) of paroxysmal tachycardia (Figures 156 and 157 pages 879 881) and of premature beats, whether of atrial or ventricular origin (Figures 154 and 155 pages 868 869) of reciprocal rhythm or ventricular escape (Figure 161 page 927) and finally of the rare atrioventricular nodal rhythm (Figure 163 page 932) In most instances of these abnormal rhythms the *P* wave does not exactly coincide either with the *QRS* wave or with the *T* wave, and so it can be distinguished. A mechanical tracing of the jugular pulse may in some of the obscure cases reveal what is

going on by the presence or absence of the a wave superimposed on the c or on the *v* (4) Finally true atrial standstill or paralysis, either transient or complete, may account for the absence of the *P* waves due to depression of the pacemaker in the sinoatrial node and to inability of the lower that is, the atrioventricular node to start an atrial contraction (see Figure 162, page 929)

Inversion of the P wave (1) Inversion of the *P* wave in Lead 2 is abnormal and occurs most commonly in the case of atrial premature beats (see Figure 154) (2) Inverted or diphasic *P* waves also occur sometimes with continuous abnormal atrial rhythms, most commonly in atrial paroxysmal tachycardia (Figure 156 page 879) (3) A third cause for inversion of the *P* wave, very much rarer than that due to atrial premature contractions or to atrial paroxysmal tachycardia, is atrioventricular nodal rhythm already mentioned (see Figure 163) Rarely an excessive irritability of the atrioventricular junctional tissue may give rise to paroxysmal tachycardia originating there. (4) A fourth cause of inversion of the *P* wave is retrogression, giving rise to a so-called retrograde *P* wave, following a ventricular premature beat.

In some instances the *P* waves are more readily studied otherwise than in Lead 2, for example, in the special atrial lead with exploring electrode in the third intercostal space at the right sternal border or in an esophageal lead when the *P* waves are indistinct or not seen in other leads.

THE ATRIOVENTRICULAR OR *P-R* (*P-Q*) INTERVAL

The *P R* (*P-Q*) interval is routinely studied in Lead 2, but observations of its length in the other leads should always be made. It is a measure of atrioventricular conduction time from the atrial pacemaker through the atrial muscle across the junction from the atrial myocardium to atrioventricular node, through this node and the bundle leading down from it, and through the right and left bundle branches and their ramifications in the Purkinje network, into the ventricular muscle fibers themselves, at which moment the *QRS* wave begins. The *P R* interval is measured from the beginning of the upstroke of the *P* wave to the beginning of the *QRS* wave, whether this be upstroke or downstroke *It normally varies in the adult from* 0 12 to 0 20 (or even in rare cases 0.21 or 0 22) second, averaging 0 16 second, and in infancy and childhood from 0 08 to 0 18 second, averaging 0.12 or 0.13 second. Its duration is undoubtedly a function of the heart size (Figure 53, page 207)

Some years ago it was demonstrated (White, Leach, and Foote, 1941) that an error may arise in the measurement of the *P R* interval, especially in Lead 2, due to the neutralization of *Q* and *R* waves in two of the three classical leads with resulting isoelectric onset of the *QRS* waves in the other lead, thus apparently prolonging the *P-R* interval. This happens most commonly when a short *Q* or *R* in Lead 1 is exactly equal in amplitude and duration to a short *R* or *Q* in Lead 3 the *P R* interval in Lead 2 is then abnormally prolonged by 0 02 or 0 03 second to include the isoelectric onset of *QRS*. Or

otherwise Q may neutralize Q_2 to prolong P-R_1, or Q_3 may neutralize Q_2 to prolong P-R_1. In occasional cases this error is clinically important when a P-R interval of 0.19 or 0.20 second is read as 0.22 second. Hence careful scrutiny for this possible error is always essential. A factor less important, which may erroneously shorten the P-R interval or neutralize the other effect, is an isoelectric beginning of the P wave.

Lengthened P-R interval. If the P-R interval is over 0.21 second, atrioventricular block is said to be present. Only very rarely is a P-R interval found to measure normally over 0.20 second, but in a few normal adults it has apparently even reached 0.22 second. The greater part of the P-R time interval is consumed in the passage of the excitation wave through the atrioventricular node and the atrionodal junction just above it (see Chapter 34). The commonest causes of prolongation of the P-R interval are active rheumatic myocarditis, coronary heart disease, and digitalis intoxication.

Shortened P-R Interval. The P-R interval may frequently appear shortened when the atria and ventricles are beating independently as in complete heart block, reciprocal rhythm, or ventricular escape, and in many instances of the ventricular premature beat. In such cases it is better to speak of the intervals between the P waves and the R waves rather than of the P-R interval as such. True shortening of the P-R interval is found in atrioventricular nodal rhythm, when the P wave, almost always inverted, falls just before, just after or with the R wave, and in that variation of normal rhythm which consists of wide QRS waves with shortened P-R intervals (of 0.1 second or less) in healthy young persons prone to paroxysmal tachycardia (Wolff, Parkinson, and White, 1930) (see Figure 168, page 953, and Chapter 34).

THE FIRST VENTRICULAR DEFLECTION OR QRS WAVE

The normal QRS wave. The QRS wave, the first ventricular deflection of the electrocardiogram and sometimes called for short the R wave, is in *Lead 2* a sharp, spike-like, monophasic, diphasic, or triphasic complex, with little or no initial downward projection known as the Q wave, a high upward projection known as the R wave, and a variable, usually slight to moderate, downward projection called the S wave (Figures 40, 42, 43 and 44). Together all components of the QRS complex should measure not over 0.1 second in duration. This first ventricular complex (QRS wave) represents the rapid activation of the entire ventricular myocardium by the excitation wave as it leaves the end branches (called the Purkinje fibers) of the special intraventricular conducting mechanism below the bundle of His. The terms dextrogram and levogram have been applied to records representing in experimental animals the primary spread of the excitation wave through right and left ventricles respectively: the addition of dextrogram and levogram results in the record obtained from both ventricles simultaneously. For the sake of convenience and uniformity it has been agreed generally to call the first upward deflection of the QRS wave the R phase or wave, any downward deflection

preceding the *R* the *Q* wave, any downward deflection following the *R* the *S* wave, and a second upward deflection following the *S* the *R'* wave if there is but one deflection downwardly directed it is labeled the *QS* wave (Committee of Electrocardiographic Nomenclature, American Heart Association, 1943). So far as time relations are concerned, the *Q* of Lead 3 may coincide with the *R* of Lead 1 and the *R* of Lead 1 with the *S* of Lead 3 the nomenclature is not concerned with time relations but rather with direction above or below the baseline.

The *Q* part of the *QRS* complex in *Lead 2* is usually absent or at most but a short point projecting 1 or 2 mm below the baseline, except in the case of infants and young children when it may form a more appreciable part of the whole *QRS* complex being as great as 3 or 4 mm in amplitude. The *R* wave in Lead 2 in the normal adult varies from 5 to 35 mm in amplitude and in infants from 5 to 10 mm. It is sharp rarely slightly notched or slurred on upstroke, downstroke, or peak. It may be the only part of the *QRS* complex present. The *S* wave is usually but a slight sharp downstroke of 1 to 3 mm immediately succeeding the *R* wave, in fact, continuous with it; it is frequently absent.

In *Leads 1 and 3* the *QRS* waves have normally less amplitude than in Lead 2. When the *R* or *S* wave occurs alone it is probable that either the other components are fused with it, or they may be isoelectric and therefore invisible in one or another lead, thus resulting in an erroneous measurement of the *QRS* duration. A narrow *QRS* wave with isoelectric onset, ending, or both, is most commonly found in Lead 2 where its apparent duration may in rare cases measure only half that of QRS_1 or QRS_3, an important error especially in the presence of bundle branch block which may be clearly evident in Leads 1 and 3 Thus all three leads must be carefully scrutinized not only to determine the correct measurement of the *P R* interval but also to learn the true *QRS* duration the widest *QRS* wave in any one of the three classical leads is the correct one, and so, as a rule, is the shortest *P R* interval. Frequently in Lead 3 but rarely in Lead 1 the phase of the *QRS* wave with the greatest amplitude is normally directed downward, whether *Q* or *S*

In the *unipolar limb leads* (Figures 42, 43 and 44 pages 190, 191 192) the *QRS* wave is normally inverted in Lead aVR with deep *Q* and small *R*, usually upright but sometimes inverted (if the heart is very vertical) in Lead aVL, and rarely normally inverted, that is, with *Q* wave, in Lead aVF there may be very small *R* and *S* waves in Lead aVF if the heart lies horizontally

In the *six unipolar precordial leads* (V_1 to V_6 inclusive) the *QRS* wave is normally diphasic with short *R* and deep *S* in the first two leads, and tall *R* and short *S* in the last two leads, with *R* and *S* of intermediate amplitudes in Leads V_3 and V_4 in other words the *R* wave increases and the *S* wave decreases as one moves from right to left (see Figures 42, 43 and 44 pages 190, 191 192) It is to be noted that in the precordial leads the peak of the *R* wave marks the time of arrival of the intrinsic excitation wave at the muscle under

lying the particular exploring electrode involved, the larger the ventricle the later and the higher the peak, while the *S* wave usually reflects the activity of the opposite ventricle *Q* waves normally are absent or small. Hence since the left ventricle is normally preponderant in size the *S* waves are larger over the right ventricle (that is, in the right precordial leads) and the *R* waves are larger over the left precordial leads. However the position of the heart enters in and may cause on occasion a very confusing picture especially if we take into account rotation of the heart around each of its three axes (Goldberger 1947) The effects of these variations of position added to the effects of disease processes and of various physiologic and toxic states comprise an extremely complicated miscellany that will require much research completely to elucidate

Abnormalities of the *QRS* wave. The *precordial leads* may show the state of different parts of the heart, in particular of the right and left ventricles, better than do the limb leads since they reflect in the main what is directly beneath them. *Thus if the right ventricle is enlarged there is a delay* in the appearance of the intrinsic deflection represented by the peak of the *R* wave in Leads V_1 and V_2 overlying the right ventricle and along with this delay frequently an increase in amplitude also. If there is right bundle branch block the intrinsic deflection is still further delayed in those leads resulting in a wide, bifid or M-shaped complex. Also if the right ventricle is enlarged there tends to be a large *S* wave in the left precordial leads over the left ventricle, that is, in Leads V_5 and V_6. Either Lead V_3 or V_4 is often a transitional point sometimes directly over the interventricular sulcus and sometimes over either ventricle and at right angles to the spatial axis as such either one is commonly used in identifying the anteroposterior plane in vectorcardiography (see page 202) In obscure cases x-ray examination and the limb leads can help a good deal.

If the left ventricle is enlarged the *QRS* waves in Leads V_5 and V_6 are altered accordingly with delay in appearance of the peak of the *R* wave (intrinsic deflection) higher amplitude of the *R* wave, and in Leads V_1 and V_2 over the right ventricle increased *S* waves. Here again displacement or rotation of the heart to the right gives much more evidence of the left ventricle in the precordial leads than usual and may be misleading. In left bundle branch block there is a much delayed intrinsic deflection peak in Leads V_5 and V_6, often giving an M shape.

The enlargement of the heart that affects the precordial *QRS* wave especially is that due to hypertrophy-dilatation also has an effect on the duration of the *QRS* wave, but manifests itself more on the *S-T* segment and *T* wave because of the abnormal myocardial condition.

It is also important to note that normally the bigger the heart, the wider the *QRS* wave without the need of postulating any abnormal delay in i-v conduction. Thus the human infant's *QRS* wave is but 0 05 second wide normally the human adult s 0.10 second, while the normal adult elephant s *QRS* wave is 0.20 second in duration (Figure 54) It would seem likely that the adult whale s *QRS* wave should be 0 4 second wide. Thus hypertrophy alone

undoubtedly gives rise to slightly increased *QRS* duration even up to 0.12 second without bundle branch block per se.

Absence of the *R* wave, leaving only a *QS* complex, is an important residual effect of a myocardial infarct underlying the particular precordial lead concerned. This finding when present is a significant clue differentiating myocardial infarction from other conditions that may produce abnormal precordial *T* waves.

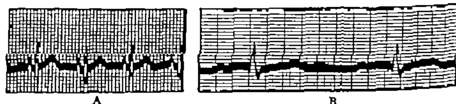


FIG 54 (*A*) Electrocardiogram (Lead 2) of normal newborn infant, B.B showing the very short time intervals *P-R*, *QRS* and *Q-T*. (*B*) Electrocardiogram of a normal middle-aged elephant, M showing the very wide time relations, a function of the size of the elephant's heart, in contrast to the time intervals of the infant's electrocardiogram. The speed of the film is the same in both (*A*) and (*B*)

An important observation that should be added concerns the amplitude of the *QRS* wave in the precordial leads. Of equal importance with actual ventricular size is closeness of the lead to the heart. Thus a thin chest wall will result in greater amplitude while a thick (e.g., obese) chest wall or fluid will decrease the amplitude.

In the *unipolar limb leads* position of the heart is particularly reflected in the *QRS* waves as well as is heart disease. In general a deep *S* wave in Lead aVR goes with left ventricular preponderance and a horizontal heart position, while a high *R* wave in Lead aVF goes with left ventricular preponderance and a vertical heart position. A *Q* wave is normally encountered but rarely in Lead aVF and an absence of *R* wave means a serious myocardial defect (an electrical hole facing the lead point, usually due to infarction).

Finally in the old "classical" bipolar limb leads despite the concentration of interest in these leads in earlier editions of this book, little can really be said about abnormalities of the *QRS* waves because of the wide range of the normal and the striking effect of varying positions of the heart. Thus the great bulk of instances of so-called *right and left axis deviations* is of physiologic interest only, associated primarily with heart position, although there are cases, of course, of extreme degree of really significant axis deviation as in the case of the tetralogy of Fallot or of the atrial septal defect. Also deep *Q* waves in Lead 1 are abnormal, usually signifying anterior myocardial infarcts, and especially prominent *Q* waves in Leads 2 and 3 generally mean posterior myocardial infarcts. And, of course, *QRS* waves over 0.12 second wide mean bundle branch block, but it is not always so easy as we used to think to tell right from left branch blocks in these leads alone. There are exceptions that are properly revealed only in the precordial leads which should always be

aken anyway in cases with widened QRS waves. As a rule it is true that wide upright QRS waves in Lead 1 and wide inverted QRS waves in Lead 3 mean left bundle branch block, the reverse being true for right bundle branch block. The last chapter in the book will have more to say about this.

The term *low voltage* has been applied to the QRS wave in particular when it has extremely small amplitude either above or below the baseline. At one time 5 mm, that is, 0 05 mv was arbitrarily selected as the borderline of normal. Inasmuch, however as normal individuals have shown amplitudes either above or below the baseline of the limb leads of 4 to 5 mm (0 4 to 0 5 mv) it is better to restrict the term "low voltage" to amplitudes of the QRS wave of 3 mm (0.3 mv) or less, especially if the low voltage involves the T and P waves too. Such low voltage has been noted in several conditions, in particular in cases of diffuse myocardial disease due to coronary atherosclerosis or other cause, extensive pericarditis acute or chronic, and rare factors as yet unexplained. In such cases the precordial leads generally show fair amplitude of the QRS waves but in a few instances they too may be much reduced and when they are, the causative abnormal conditions are usually of greater degree. The voltage, however of the QRS waves in the precordial leads is affected also by distance of the electrode from the heart. Thus, an extensively fat chest wall or much fluid or air interposed between the heart and chest wall are factors that reduce the precordial QRS voltage.

Alternation of the amplitude of the QRS waves without other change (that is, without alternating change of shape or of time interval) is exceedingly rare I have seldom encountered it in the past 30 years. A few years ago two cases were reported, the first case being the only one found in a series of approximately 10 000 electrocardiograms taken over a period of 13 years (Hamburger Katz, and Saphir 1936) the prognosis is apparently bad as in the case of the ordinary pulsus alternans. On the other hand, alternation of the arterial pulse is common and is attended in only the rarest cases by electrocardiographic alternation, either of QRS waves or T waves, or both.

THE *S-T* SEGMENT

Immediately following the onset of systole that is, after the QRS wave, there is usually in the normal subject a short isoelectric interval showing itself electrocardiographically as the S-T segment following the S-T junction. Both the segment between the S and the T waves and that of the T wave itself are easily susceptible to modifying influences, physiologic effects, structural changes, anoxia, and myocardial infection and poisoning, which may produce changes of shape and amplitude. The S-T segment and the T wave represent simply phases of the same electric process, repolarization during cardiac systole. The S-T junction and S-T segment may be normally slightly elevated, up to 1 mm in limb leads and to 2 mm in precordial leads.

Changes in the S-T segment There are frequent changes in the S-T segments which accompany abnormalities of the T waves themselves but which

actually may be more important in the information they yield about the myocardium they are as a rule temporary however subsiding when toxic influences and currents of injury subside. The most common and most striking S T segment abnormalities are those associated with digitalis intoxication and with myocardial infarction and ischemia (most commonly from coronary disease rarely from trauma or a state of vascular shock or anoxia) acute pericarditis with its associated subpericardial myocardial involvement may elevate the S T segments appreciably especially in Leads 1 and 2 and in the precordial leads involved. With full digitalization the S-T segment of Leads 1 2, and 3 and of the multiple precordial leads is considerably depressed, and is said to sag," dropping sometimes several millimeters below the baseline so that the T may arise very low and be diphasic or in extreme cases totally inverted (see Chapter 30) This digitalis effect is in contradistinction to the findings in acute myocardial infarction and ischemia when the S-T segments are depressed or raised from the baselines in the opposite direction to the T wave changes that is, early in the anterior wall type of infarction the S-T segment is elevated in Leads 1 V_4 and V_5 and depressed in Lead 3, and vice versa in posterior wall infarction type these changes are transient, persisting as a rule but a few hours or days (see Chapter 21) The S-T segment tends to be markedly elevated in the multiple precordial leads over the region of the fresh anterior infarct, while it may be considerably depressed in cases of acute posterior infarction (see Chapter 21) Also injury at the endocardial surface of the left ventricle may cause depression of the S-T segments in the precordial leads over the left ventricle in contrast to the effect of the more usual subpericardial lesions. In the case of large chronic myocardial infarcts, usually associated with cardiac aneurysms, the S-T segments may be permanently displaced (e.g. elevated in Leads 1 V_4, and V_5 in the case of large anterior aneurysms)

Infectious changes, other toxic poisoning of the myocardium, and hyperventilation may sometimes affect the S T segment, but rarely as much as does acute infarction or digitalization hypothyroidism has but little effect on the S T segment while flattening out the T waves. In some cases of left ventricular enlargement (or strain) there is a slight depression of the S-T segment in Lead 1 even when there is no left axis deviation (Barnes, 1940) In fact it is now well recognized that S-T segment depression in Lead 1 and in Leads V_4 and V is more characteristic of the effects of strain on the left ventricle than is left axis deviation this simulates the effect of anoxia in acute coronary insufficiency

THE SECOND VENTRICULAR COMPLEX OR T WAVE

The normal T wave. The T wave or second ventricular wave of the normal electrocardiogram is in Lead 2 a blunt, rounded, upright deflection following the S-T segment, beginning gradually from the isoelectric baseline a short but variable distance, about 0 05 to 0 15 second, after the end of the QRS wave, rising to a height of 2 to 10 mm usually 3 or 4 and sloping somewhat more

sharply downward to the baseline again, to end about 0.25 to 0 30 second after the end of the normal *QRS* wave (Figures 42, 43 and 44) The duration or width of the *T* wave thus varies greatly from about 0 10 to 0 25 second. It falls during ventricular systole, ending with the end of systole and the occurrence of the second heart sound. It has been variously explained, probably best as the repolarization (recharging) of the myocardium as contrasted with the depolarization (electric discharge) of the myocardium represented by the *QRS* wave. The *T* waves in Leads 1 and 3 are normally of less amplitude as a rule, than the T_2 wave: T_1 is low (about 1 or 2 mm) but almost invariably upright normally while T_3, also of low amplitude, may be normally upright, flat, or even inverted. The *T* waves in the unipolar limb leads vary from normally inverted in aVR to upright or inverted in aVL and aVF depending on the position of the heart, tending to be inverted in aVL and upright in aVF in the case of a vertical heart and upright in aVL and low but not inverted in aVF in the case of a horizontal heart. The *T* wave in precordial Leads V_3 to V_6 inclusive is almost always upright (about 3 to 6 mm) in the normal adult, but in the young child it may be inverted normally The *T* waves vary from very low flat, or inverted in V with increasing amplitude to high (5 to 10 mm) in V_3 and V_4, to lower levels in V_5 and V_6, they should not normally be inverted in the adult except in V and V_2

Physiologic variations of the T wave As stated above the *T* waves in Lead 3 normally vary widely from upright to inverted, depending in large part on position of the heart as affected by the height of the diaphragm in opposite phases of respiration and in opposite body builds: thus, in full inspiration and in the case of a vertical heart the *T* waves in Lead 3 tend to be upright in direction with a swing of the electric (and anatomic) axis toward the right, while in full expiration and in the case of a horizontal heart the *T* waves in Lead 3 tend to be inverted with a swing of the axis toward the left (see Figure 4 page 33)

Until recent years, however flattening or inversion of the *T* waves in Leads 1 2, and V_3 to V in the adult has been attributed to actual heart disease. In Leads 1 and V and V such a surmise is almost invariably correct so far as we yet know with very rare exceptions due to the same factors, namely heart position and autonomic nerve influences, which can be responsible in the case of the far more numerous exceptions found in Lead 2.

Occasionally flattening, notching, or even inversion of the *T* waves in Lead 2 may be a positional effect in normal individuals in such cases a vertical heart position in a long thorax with tendency to right axis deviation is attended in the sitting or standing position by notched, diphasic, or inverted *T* waves which assume the usual normal upright appearance in the recumbent position or on deep expiration (with or without much of any change in axis deviation of the *QRS* waves on changing position, rotation of the heart probably playing the important role) It is important to recognize this normal variation, which has frequently in the past been attributed to myocardial disease (see Figures 5 and 6, page 34 and page 35) (White, Chamberlain, and Graybiel, 1941) In very rare cases even *T* may be normally inverted when the heart is

unusually placed vertically with the *T* in aVL deeper than in aVR, or horizontally with marked clockwise rotation.

In addition to the effect of position, autonomic nerve impulses may affect the *T* waves in Lead 2. Sympathetic stimulation as *during* exercise and from fear or adrenaline, and vagal inhibition, as from atropine lower the *T* waves even to the point of inversion (Figure 55) (Hartwell, et al 1942) while

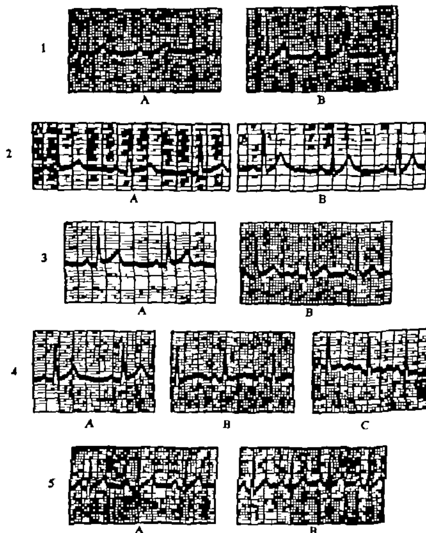


FIG. 55 Changes in the *T* waves of the electrocardiogram resulting from the action of certai drugs, in particula ergotamine, atropine, and adrenaline, and of exercise (during and after) Note the increase in the *T* waves by vagus stimulation as evidenced by (1) the action of ergotamine and (2) the after-effect of exercise nd the depression of the *T* waves as the result f sympathetic nerve stimulation or preponderance as evidenced by the effect of (3) atropine, (4) adrenaline, and (5) exercise itself directly. All tracings are of Lead _ (*A*) control record (*B*) records at height of effect; (*C*) shows maximal adrenaline effect—drug given intravenously (Hartwell, Burrett, Graybiel, and White, *J Clin. I estigation* 1942, XXI, 409)

vagal stimulation, as from ergotamine and *after* exercise, raises the *T* waves (Figure 55)

Abnormalities of the *T* wave. *Increase in amplitude of the T wave* The end of the *T* wave of Lead 1 tends to become higher in cases of posterior myocardial infarction due to coronary thrombosis in contrast to late inversion of the *T* wave in Lead 3 while the reverse is true, that is, there is a late increased elevation of T_3 when there is late inversion of *T* in the cases of anterior wall infarction. In the old Lead 4 and in the multiple precordial leads over the left ventricle V_4, V_5, and V_6, the *T* may remain unchanged or become higher than normal in the posterior wall infarction it is almost always considerably inverted in the anterior wall infarction (see Chapter 21) especially in chest Leads V_4 V_5, and V_6. In cases of lateral wall infarction it may be inverted in Lead V_6 only

In the electrocardiograms of premature beats, marked axis deviation, and bundle branch block, the *S-T* segment and *T* wave are usually widely deviated from the baseline in the opposite direction from that of the abnormal *QRS* wave, thus giving sometimes very high *T* waves. A similar opposite direction of *T* wave from *QRS* wave in Leads 1 and 3 helps to separate the marked axis deviation due to pathologic cardiac conditions from left axis deviation of lesser degree which may be due to change in position of the heart (when the *T* wave tends to take the same direction from the baseline as does the *QRS* wave) Thyrotoxicosis, sometimes stated to show a *T* wave increase, is, as a matter of fact, generally without appreciable effect or has an opposite effect, even to flatten or invert the *T* wave, doubtless due to the sympathetic overstimulation.

Decrease in amplitude and inversion of the T wave Decrease in amplitude of the *T* waves from the normal and their inversion in disease are found under several conditions. In Lead 2 decrease in amplitude is frequently present in marked left or right axis deviation or even in right or left bundle branch block, along with a diphasic character of the *QRS* wave due to the neutralizing effect of Leads 1 and 3 on each other In general, however flattening and inversion of the *T* waves in the three classical leads are most commonly the result of digitalis action, of myocardial ischemia or infarction from coronary disease of acute pericarditis or chronic constrictive pericarditis, of infectious myocardial involvement, and of hypothyroidism (myxedema or cretinism) There are differences between the effects of these five clinical conditions. In the multiple precordial leads the *T* waves vary according to the part of the heart affected, but are influenced like the limb leads by general factors such as digitalis, myocarditis, and myxedema.

1 Digitalization usually causes a decrease, leading to flattening or even, in extreme cases, to deep inversion, of the *T* wave following a sagging of the *S-T* segment (see Figure 158 page 897 and Chapter 30)

2 The *T* wave of myocardial ischemia or infarction due to coronary disease or insufficiency tends *to be flattened or inverted in Lead 2 but varies in* the other leads according to the site of the maximum amount of myocardial

change. It is at first slightly elevated, along with the *S T* segment, in Lead 1 with or without very slight late inversion (Pardee's sign, Pardee, 1920) during the most acute stage of anterior wall type of myocardial infarction (due probably to a "current of injury" at the left ventricular apex) but it becomes usually sharply inverted after a few days, remaining inverted for weeks, months, or years. When there is chronic coronary insufficiency with or without actual old infarction, involving a large area of the left ventricle toward the apex, the *T* waves in Leads 1 and V_4 and V_5 are usually flattened or inverted in their terminal portions. In cases of anterior wall myocardial infarction or left ventricular basal ischemia the same statements just made concerning T_1 apply to the *T* waves in Lead 3 instead. In the multiple precordial leads the *T* waves are unchanged or heightened in the case of the posterior wall infarction or left basal ischemia and flattened or inverted (often deeply so) over the left ventricle in the case of anterior infarction or left apical ischemia. When there are multiple areas of infarction or ischemia there are multiple effects on the electrocardiogram which are often confusing; perhaps the simplest combination is inversion of the *T* waves in Leads 1, 2, and 3 with diphasic *T* waves in the precordial leads over the left ventricle when there are comparable infarcts at both apex and base (see Chapter 21)

In the multiple precordial leads inversion of the *T* waves over the right side of the precordium and not over the left indicate enlargement of or damage to the right ventricle or infarction of the interventricular septum, while inversion of the *T* waves over the extreme left side of the precordium indicate infarction or other damage of the lateral wall of the left ventricle

3 With pericarditis, especially when there is acute or chronic constriction of the heart and great vessels, the *T* waves tend to become flattened or, more often, inverted in all leads, after temporary elevation of the *S-T* segments, but especially in Leads 1 and 2, for some days in the early stages (see Chapter 27)

4 With serious infections there are occasionally observed changes in the *T* waves consisting of decrease in amplitude, flattening, or inversion in both limb leads and multiple precordial leads, similar to those just recounted as sometimes occurring in pericarditis these changes are due to acute myocardial involvement and are particularly likely to occur in rheumatic fever, diphtheria, and pneumonia, and sometimes in virus diseases. The same effects are due rarely to noninfectious poisons (other than digitalis which has been mentioned above) as from tobacco (see Chapter 23)

5 The *T* waves of hypothyroidism are very low absolutely flat (most commonly) or even inverted in all leads they resume a normal amplitude after thyroid therapy (see Chapter 18)

There are other rare instances of depression or inversion of the *T* waves of uncertain or unknown nature and even an individual who is apparently normal may temporarily show this finding due, as a rule, to unusual heart position or nerve influence (see Figures 5 page 34 and 55 page 218 for example)

The *T* wave is frequently diphasic but rarely notched. Its diphasic character results often from the inverted nature of the *S-T* segment which merges into the slightly upright *T* wave, as in digitalis action occasionally the diphasic sequence is the reverse, first upright, then inverted, as in cases of cardiac infarction. A late notch or dip in a low *T* wave in Lead 2 suggests the effect of heart position in an otherwise normal person in the sitting position In such a case a further electrocardiogram should be taken with the subject recumbent or in full expiration to correct the effect of the heart s unusual angle or rotation.

Alternation of the *T* waves in amplitude alone, like alternation of the *QRS* waves, is very rare it may accompany alternation of the arterial pulse, as a serious sign.

THE *Q-T* DURATION

The time interval from the onset of the *QRS* wave to the end of the *T* wave can be taken to measure quite accurately the duration of ventricular systole, when the deflections are clearly marked so that the end points are readily seen. With good technic this so-called *Q T* duration of the electrocardiogram is the best measure we possess for the length of systole. With clear curves, measurement by the Lucas comparator gives an error under 0 01 second. The *Q-T* duration (duration of systole) varies primarily with the heart rate, being shorter with faster rates and longer with slower rates, about 0 35 second at a heart rate of 75 0.25 second at a rate of 120 and 0 45 second at a rate of 45 The *Q-T* duration varies abnormally only in some cases with high-grade atrioventricular and intraventricular block in ventricular premature beats, in hypocalcemia and hypopotassemia, and with marked enlargement (especially dilatation) of the heart, in which conditions it is longer than the outer limit of the normal, in heart failure a prolonged *Q T* duration (systole) is shortened by an adequate digitalis effect. With respect to heart size it is of considerable interest that the duration of systole (the *Q T* duration) of the elephant's heart is, relative to heart rate, much longer than that of the human heart (White, Jenks, and Benedict, 1938) (Figure 54 page 214) and one might justly prophesy that the whale s *Q T* duration, like other time intervals, would be similarly relatively prolonged.

THE *U* WAVE

Occasionally in Leads 1 and 2 and frequently in the precordial leads there occurs normally a slight upright deflection, a small wave usually less than 1 mm high but sometimes higher immediately following the *T* wave, and therefore appearing in early diastole (Figures 40, 42, 44 and 53) This is called the *U* wave. Its significance is unknown, but it is probably representative of some diastolic electric process in the myocardium, since it is more evident after a high or deep *T* wave than at other times and since it tends to be inverted when the *T* wave is inverted. The *U* wave is apparently of little clinical

importance except that it may be abnormally inverted when the T wave is upright and that it may be confused with the P wave or more commonly with the end of the T wave, in which latter case it may be wrongly interpreted as a notching of the T such an error can be avoided by a measurement of the expected Q-T interval at the heart rate recorded.

Serial electrocardiograms. In closing this chapter I would like to emphasize the great importance of serial electrocardiography Repeated records are often essential for the diagnosis of such acute conditions as myocardial infarction, acute pericarditis, and the acute cor pulmonale Annual, monthly weekly daily or even hourly records may reveal much more than any single electrocardiogram Also every young person while in good health should have a routine electrocardiogram taken for future reference just as he or she should also have a chest x-ray film.

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CHAPTER 10

OTHER METHODS OF EXAMINATION

INTRODUCTION

The patient's history, physical examination, electrocardiogram, and roentgen ray study have been discussed in the earlier chapters of this book and have been roughly appraised in value as parts of the complete clinical examination in the order of about 45, 25, 15, and 10 per cent respectively. These percentages add up to 95, leaving the remaining 5 per cent to be divided up among all the other methods of examination which include the technic of cardiac catheterization and the testing of blood, urine, strength and endurance, vital capacity and other respiratory functions, blood flow, circulation rate, and work of the heart and of the pulse. Various other tests of less immediate or routine cardiovascular importance, such as the basal metabolic rate and sputum and gastrointestinal examinations, are not included in this chapter but are referred to later in appropriate chapters. Any one of these methods of examination may, however, uncover a vital clue, and so they must all be borne in mind and turned to at once in case of need. Many of the additional tests, such as ballistocardiography, the discussion of which has been transferred to a more appropriate chapter (Chapter 8), are of much academic interest and worthy of use in special investigations; a few may some day assume practical importance in clinical medicine related to the heart and great vessels. As a whole, however, at the present time the methods discussed in this chapter are infrequently of prime importance in cardiovascular diagnosis, although they may be invaluable in the execution of special research.

CARDIAC CATHETERIZATION

Forssmann, W. "Die Sondierung des rechten Herzens." ("Sounding the Right Heart.") *Klin. Wchnschr.* 1929, VIII, 2085.

Shortly after the publication of this paper Dr. Forssmann's attention was called to an earlier publication on catheterization of arteries in the human for the purpose of therapy (Bleichröder, Unger, and Loeb, "Intraarterielle Therapie." *Berl. klin. Wchnschr.* 1912, 3). However, this earlier work apparently did not include catheterization of the heart per se and was not followed up by further research or application.

"Following the successful investigations in the cadaver I undertook the first study in living man in the form of a *research on myself*. Next I arranged in a preliminary test to have my right elbow vein punctured with a thick needle by a colleague who kindly placed himself at my disposition for this purpose. I introduced then, as in the case of the researches on the cadaver, a well-oiled ureteral catheter of 4 Charrières thickness through a cannula into the vein. The catheter allowed itself to be introduced very easily to a length of 35 cm. Since going further seemed too dangerous to the colleague we stopped the investigation at that point even though I myself felt quite well. After a week I undertook a further investigation alone. Since a puncture of the vein with a thick needle on my own body was technically too difficult, I made under local anesthesia a venesection in my left elbow and introduced the catheter without any resistance in its whole extent of 65 cm. This length appeared to me, after measuring the surface of the body, to agree with the distance from the left elbow to the heart. On introduction of the catheter I had, during the procedure, merely a feeling of slight warmth in the wall of the vein similar to the sensation after intravenous injection of calcium chloride. On backward movement the catheter touched the upper and lower wall of the subclavian vein. I then felt an especially intensive warmth behind the collar bone under the insertion of the sternocleidomastoid. Simultaneously, doubtless through the stimulation of the vagus branches, I felt a slight tendency to cough.

"*The position of the catheter* I confirmed *in a Röntgen photograph* and observed the shadow of the catheter itself by means of a mirror held by a sister before the fluoroscopic screen. (Translation by myself.)

Thus in 1929 Forssman successfully catheterized his own heart by way of an arm vein. Considered a bold and dangerous procedure at first, it has, in the last few years, become a commonplace, though still a delicate, method of study of the right heart chambers and pulmonary arterial circulation, particularly in congenital cardiovascular disease and in measurement of the pulmonary blood pressure, a longfelt want now at last realized (Figure 56). It is very important, wherever cardiac catheterization is carried out, to establish a well-trained team of workers to ensure proper technic and adequate recording; such a team usefully includes cardiologist, roentgenologist, cardiovascular surgeon, and physiologic technician. It is well to record the blood pressure in the superior vena cava, in the right atrium, in the right ventricle, and in the pulmonary artery and its main branches, by Hamilton manometer or by the newly introduced electromanometer (see Chapter 6). Samples of blood for determination of oxygen content are taken similarly from these various sources to determine if possible the entrance of oxygenated blood through atrial septal defect, ventricular septal defect, or patent ductus arteriosus (see Chapter 13). The course of the specially modified ureteral catheter, 100 to 125 cm in length, can be followed fluoroscopically as it passes from one chamber to another or in abnormal hearts into left atrium or aorta, and x-ray films can occasionally be taken. It is possible also to use such a catheter to explore

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Also Forssmann mentioned the fact that Christaller and Ebner had used Unger's arterial method in animal experimentation. Forssmann refers to these two earlier communications in short statement in the *Klin. Wchnschr.* 1929. VIII, 2287.

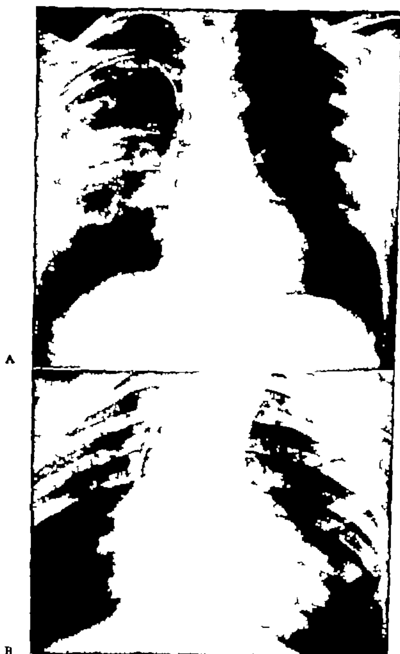
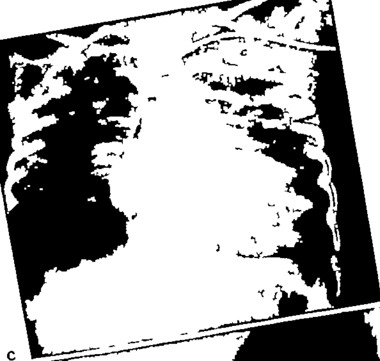


FIG. 56 X-ray films of thoraces with catheter in heart. (*A*) Normal heart. C theter is seen entering the right atrium from the perior vena cava ad its tip can be noted in the right pulmonary artery (*B*) Atrial septal defect with pulmonary stenosis. The catheter is seen to pass from the right atrium through the septal defect to the left atrium and into a right pulmonary vein. Not the lower position of the pulmonary vein in contrast to that of the artery



C

D

(*C*) Large patent ductus arteriosus. The catheter is seen to pass from the main pulmonary artery through the ductus and down the descending aorta. (*D*) Tetralogy of Fallot. The aortic arch is right-sided. The catheter is seen entering the aorta from the right ventricle. (Kindness of Drs. Gordon S. Myers, Massachusetts General Hospital, Boston; Bernard J. Walsh, Washington, D.C. and Lewis Dexter, Peter Bent Brigham Hospital, Boston.)

the coronary hepatic, and renal veins and determine blood gases to study local organ metabolism. Finally it is possible by the insertion of a special wire and electrode through the catheter to obtain right intra-atrial and intraventricular electrocardiograms, which, as yet, have been largely of academic interest (see Chapter 9.)

In normal individuals the blood pressure in the superior vena cava has been found to be about 3 mm Hg, in the right atrium 0 in the right ventricle 20 to 30 mm systolic and 0 diastolic, and in the pulmonary artery 20 to 30 mm systolic and 5 to 10 mm diastolic. With the catheter tip as far as possible in the pulmonary vessels an essentially capillary oxygen reading can be secured.

The oxygen content of blood samples taken from the superior vena cava and right atrium may vary considerably since the venous blood from various sources has not yet been well mixed. For example, a sample taken near the coronary sinus may have an oxygen content as low as 3 or 4 volumes per cent. Mixing is more complete in the right ventricle and pulmonary artery where the oxygen content usually measures between 10 and 14 volumes per cent.

Under abnormal conditions with congenital septal defects and patent ductus arteriosus there are increased blood oxygen contents in the right atrium, right ventricle, and pulmonary artery according to the position of the left-right shunt pulmonary vascular involvement and certain heart conditions may elevate the pressure readings, even to levels as high as three or four times the normal.

TESTS INVOLVING THE USE OF RADIOACTIVE ISOTOPES

Cutting across various special fields of internal medicine and applicable to a variety of tests in such fields has been the introduction of radioactive isotopes in the years that have followed World War II. Even in therapy also this newly acquired knowledge has played a role particularly in the form of irradiated iodine to reduce the activity of the abnormal thyroid gland in thyrotoxicosis or of the normal thyroid in combating intractable angina pectoris or congestive failure (a "medical thyroidectomy") But radioactive isotopes have played a role much more prominently in diagnosis and research than in therapy in cardiovascular disease. In 1942 Hubbard, et al., used radioactive sodium to determine the velocity of blood flow in infants and young children. This has been followed up since by Prinzmetal, et al. (1949) who have applied the method to adults. In 1945 Nylin reported the determination of the circulating blood volume by the application of the new method worked out by Hevesy wherein blood corpuscles were tagged with radioactive phosphorus and the time of equilibrium of their dilution curves established by the use of the Geiger counter In normal cases the circulating blood corpuscles averaged 33 4 gm per kilogram of body weight while in heart failure there was a considerable increase with return to normal figures when the failure cleared in one case there was a drop of 28 per cent when congestion disappeared. Using the same technic, Nylin (1947 1948) has

studied the corpuscular and total blood volume in various organs, including the lungs and the heart· he found, for example, that 17 per cent of the total circulating blood volume was to be found in one lung and 13 6 per cent in the lower limbs. Dow et al. (1946) and Gibson, et al. (1946) used radioactive isotopes of iron similarly to measure the circulating red cell volume. Prinzmetal, et al. (1947) studied the collateral circulation of the normal human heart by coronary perfusion with radioactive erythrocytes and glass spheres, and later (1949) used a specially constructed ink-writing Geiger Mueller counter to record the passage of radioactive blood through the heart chambers, which they called radiocardiography" Burch, et al. (1947) have used radioactive sodium to study congestive heart failure, and Smith and Quimby (1947) Elkin, et al. (1948) and Wright, et al. (1948) have used radioactive sodium to study the peripheral circulation.

EXAMINATION OF THE BLOOD

Blood examination affords a wealth of data concerning its various constituents and properties, which are sometimes of much value in the study of a patient with cardiovascular disease.

Hemoglobin. Usually the hemoglobin in cardiac patients is within normal limits, 80 to 90 per cent by various methods (13 to 15 gm per 100 cc of blood) Slight anemia, down to 70 or even 60 per cent hemoglobin, may occur in severe or long-continued acute rheumatic heart disease. Moderate to severe anemia, down to 55 or even 40 per cent hemoglobin, is sometimes present in subacute bacterial endocarditis, although slighter grades are more common. The discovery of a low hemoglobin content due to hypochromic anemia of noncardiac origin or to primary pernicious anemia may prove helpful in explaining not only systolic but also diastolic heart murmurs due to cardiac dilatation resulting from the anemia. Sometimes the differential diagnosis between anemia secondary to bacterial endocarditis and that secondary to other factors is difficult. An abnormally high hemoglobin content, over 100 per cent, is found with polycythemia resulting from congenital heart defects which are attended by cyanosis and a right to left shunt of blood. This percentage of hemoglobin may be as high as 150 (22 gm) or more. Polycythemia vera may in turn be itself a factor of circulatory strain (see Chapter 23)

Recently an iron pigment in muscle, called myoglobin which, like hemoglobin, has a function of picking up and storing oxygen has been under investigation (Blörck, 1948) but further study is needed to ascertain the clinical significance of variations of its amount in heart muscle

Red blood cells. The red blood corpuscles are decreased below the normal in number relatively less than is the hemoglobin in the anemia of acute rheumatic heart disease and in that of subacute bacterial endocarditis, as in almost any secondary anemia. They usually vary between 3 000 000 and 4,000 000 per cubic millimeter according to the severity of the anemia, rarely falling to 2,500,000 or 2,000,000 or below in the severest grades of anemia found in

bacterial endocarditis. In contrast in the morbus caeruleus of congenital heart disease the red cell count is as high as 6 000 000 to 12,000 000.

White blood cells. In infections of the heart the white blood corpuscle counts are increased. A slight leukocytosis with a total count of 10 000 to 15,000 per cubic millimeter and a polymorphonuclear percentage of 70 to 85 is common in acute endocarditis rheumatic or otherwise, although frequently in mild cases the number of white blood corpuscles is normal in the more severe and fulminating cases of bacterial endocarditis with complications such as embolic infarcts it can be much greater even to a total white count of 30 000 with 95 per cent polymorphonuclear cells. Cardiac infarction from coronary thrombosis or embolism usually results in polymorphonuclear leukocytosis for a few days, from a slight degree (12,000 with 75 per cent polymorphonuclear cells) to a high degree (25 000 with 90 per cent polymorphonuclear cells) depending on the size of the infarct. A small infarct may result in no obvious leukocytosis.

Sedimentation rate. The rate at which the sediment of nonclotted blood settles out is much increased in many disease conditions, including the infections involving the heart (rheumatism, bacterial endocarditis, and tuberculous pericarditis, for example) and myocardial infarction from coronary thrombosis. It is a useful test, not in differential diagnosis but in helping to determine when an active process has completely subsided, particularly subacute rheumatism, infectious activity in a constrictive pericarditis, and active tissue replacement in myocardial infarction. It is important to correct the sedimentation rate index for marked variations in the cell volume percentage (hematocrit) of the blood, for example, a fast rate of 0.5 mm per minute (in a 100 mm sedimentation tube with heparinized blood) in a case with severe anemia may be corrected to a "normal" rate of 0 25 mm per minute found when the hematocrit is normal (at 45 per cent) (Rourke and Ernstene, 1930)

Blood culture. Bacteriologic examination of the blood is occasionally helpful in endocarditis. The smear shows no organism, but a culture, when enough blood, 5 to 20 cc, is taken and the culture medium, hormone broth with a hydrogen ion concentration of *p*H 7 6, is carefully prepared, should reveal the presence of the Streptococcus viridans in the great majority of cases of subacute bacterial endocarditis. Sometimes several cultures must be taken before positive ones are secured. At least three or four positive cultures are essential for complete confirmation of the diagnosis of subacute bacterial endocarditis one or even two positive cultures may be more or less accidental findings. Cultures are also useful in determining the particular organism, streptococcus, staphylococcus, pneumococcus, gonococcus, or rarer bacteria responsible for acute bacterial endocarditis. Infrequently in rheumatic endocarditis streptococci have been found in blood cultures, and sometimes are thought to be responsible for the infection, but blood cultures positive for streptococci have similarly been found in various other diseases and even in relatively normal controls, especially when there are chronic foci of infection, particularly dental, and immediately after tooth extraction (not particularly

after tonsillectomy) This finding is best interpreted as indicating that occasionally stray bacteria may invade the blood stream without causing disease, except in rare hearts where there may be suitable soil for their growth as in the case of subacute bacterial endocarditis.

Serologic reactions. Although on rare occasions such serologic tests as those for the gonococcus or the echinococcus may be helpful, if carefully carried out, it is only the Wassermann or allied (Kahn or Hinton) reaction for syphilis that is of routine value. Because of the relative infrequency of cardiovascular syphilis in certain communities, this reaction will prove negative in most cardiovascular patients in those communities, but in other parts of the world where syphilis is rife and its treatment inadequate a positive Wassermann reaction will be commonly found. When it is positive the test is of help in confirming a diagnosis of cardiovascular syphilis made on other grounds, or in calling attention to its presence. When negative this test for syphilis is of only limited value, although the great majority of all patients with cardiovascular syphilis (about 85 per cent) yield positive Wassermann or Kahn or Hinton reactions. Even when positive, the reaction may be misleading, for nonsyphilitic heart disease and incidental syphilis may be present in the same patient; also other conditions like jaundice and subacute bacterial endocarditis may rarely yield slightly positive reactions. These facts must be remembered and great care and judgment exercised before a positive Wassermann reaction is allowed to influence diagnosis, prognosis, and treatment; there may be a justifiable suspicion of cardiovascular syphilis but symptoms or signs are essential to establish the diagnosis.

Viscosity of the blood. Viscosity of the blood, chiefly dependent on its cellular content, is rarely an important factor so far as the circulation is concerned, and its measurement is largely a matter of academic interest. Occasionally however its increase, as in high-grade polycythemia, where it may be as much as three times the normal, is a distinct burden for the circulation and a threat for thrombosis it has to be offset in part by capillary dilatation. Decreased viscosity occurs in anemia and temporarily in congestive failure or with forcing of fluid intake

Chemical analyses. Certain chemical analyses of the blood have become of routine value in internal medicine, including cardiovascular disease. An excess of nonprotein nitrogen beyond the normal upper limit of 40 mg per 100 cc of blood, or of urea nitrogen beyond 20 mg per 100 cc, means nitrogen retention which in turn means renal insufficiency but usually not primarily renal disease in cardiac patients congestion from heart failure may be the cause. An abnormal increase is an accompaniment also of uremia, which may act to poison the heart, and of a renal shut-down due to dehydration. The amount of blood sugar normally not over 120 mg per 100 cc of blood, is worth knowing when diabetes mellitus is suspected, because of the frequent association of this disease with early arteriosclerosis, and because of its unfavorable effect on heart disease but too low a blood sugar (as from excess of insulin) may also act harmfully in acute coronary heart disease.

The serum content of albumin and globulin in relation to cardiovascular disease has not been shown to be of clinical importance in the differentiation of cardiac edema from the edema due to liver disease or to malnutrition. Any one of these factors may complicate the others. In heart failure the serum protein is usually normal, in the other two conditions much lowered (to 5 0 gm per 100 cc or less) especially in its albumin fraction. Although it is possible to measure the contents of various ions in the serum (e.g., sodium—normally 136–145 meq per liter potassium—3.5–5 0 meq per liter calcium—9 0–10.5 mg per 100 cc, and chloride—100–106 meq per liter) much still remains to be learned about the significance of the blood content of salts and their elements, acid and base, along with the hydrogen ion concentration, which remains strikingly constant (7 35 to 7 45) through buffer action. Suggestions of the significant effect that may result from abnormality of such relationships is shown, however in an unusual elevation of the *T* waves of the electrocardiogram in acidosis and in the case of a high potassium content (which may also induce or favor the occurrence of heart block—Thomson, 1939) and depression of the *T* waves in alkalosis and low blood potassium, as well as in the case of hypocalcemia (in tetany) in which with very low blood calcium (4 to 5 mg per 100 cc of blood) the duration of systole as measured electrocardiographically is prolonged appreciably beyond the normal, dropping again within normal limits when the blood calcium is restored to normal (10 mg) It is also important to remember that the serum content of salts does not indicate the intracellular chemical status. Finally there are other substances for which, on occasion, the blood should be analyzed, e.g., cholesterol in coronary heart disease and thyroid diseases especially (normally 150 to 250 mg per 100 cc serum) and vitamins in suspected avitaminosis (A normally 40 to 100 units per 100 cc, C normally 0 4 to 1 0 mg per 100 cc)

Oxygen in the blood. The normal content of oxygen in arterial and venous heart blood, measured in terms of percentage saturation (if all the hemoglobin were oxygenated the saturation would be 100 per cent) is 95 per cent saturation (18–21 volumes per cent) for arterial blood and about 70 per cent saturation (10–16 volumes per cent) for venous heart blood. For certain parts of the body the venous blood will show a greater degree of unsaturation, but this excess is neutralized in the venous heart blood by a lesser degree of unsaturation in other parts of the body Stasis of varying degree and increased tissue metabolism account for the differences. The more active the metabolism and the greater the stasis anywhere, the less oxygen remains in the blood and the bluer it becomes. The dissociation of oxyhemoglobin, however requires a favorable temperature, and if the air is very cold so that the skin is chilled, the peripheral skin circulation, although greatly slowed, gives not a blue but a red color due to the presence of unreduced oxyhemoglobin.

A helpful instrumental device, called the oximeter (Millikan, 1932) for the photoelectric determination of blood oxygen saturation in man by standardization against known blood samples, can be applied to the ear or even to whole blood via cardiac catheter

A decrease in amount of oxygen saturation of arterial blood can be of degree; it has been found to be as low as 58 per cent in a case of our of congenital heart disease with the tetralogy of Fallot and marked cya- (Talbott, et al., 1941) 32 per cent in a cyanotic and fatal case of the influenza epidemic of 1918–1919 (Stadie, 1919) and even per cent in a case of bronchopneumonia, with increase to 79 per cent through oxygen inhalation (Meakins and Davies, 1925) A decrease in oxy gen saturation of arterial blood is due to any one of eight factors, as listed herewith. (1) Pulmonary congestion from heart (left ventricular) failure may be so great that in the distended pulmonary capillaries much venous blood passes through without contact with the alveolar wall and the oxygen on the other side of that wall also moisture in the alveoli may prevent the proper entrance of air (2) Pulmonary vascular engorgement from mitral stenosis, without real heart failure, acts in the same way (3) Pneumonic or other consolidation, which causes a shunt of venous blood to the left heart through the capillaries of solid lung into which little or no air and oxygen can pene- trate, may also reduce the oxygen content of arterial blood. (4) Destruction of a large amount, over half, of the total lung tissue may prevent sufficient air from reaching the pulmonary circulation. (5) Chronic emphysema and asthma, in which the respiratory exchange is very limited, may also prevent sufficient oxygen from reaching the alveoli and blood stream. (6) High alti- tudes, 10,000 ft (about 3 000 meters) and over where the oxygen content of the inspired air is low do not allow a completely normal oxygen saturation of the blood. At 14,200 ft elevation the oxygen saturation of the arterial blood has been found to vary between 80 and 90 per cent instead of the normal of 95 per cent or slightly more (Barcroft and associates, 1922) and at 17,500 ft the variation was from 67 6 to 84 6 per cent (average 75 per cent) in six resident healthy workmen (Talbott and Dill, 1936) (7) Poisoning by carbon monoxide or other toxic agent to cause methemoglobinemia may prevent some of the hemoglobin from taking up oxygen in the lung. (8) Congenital heart disease may be attended by shunts, that is, through atrial or ventricular septal defects, large enough to allow a considerable amount of venous blood to cross directly into the arterial circulation without first going through the lungs. Con- genital transposition of the aorta and pulmonary artery may also be a cause.

Three additional observations about blood oxygen are of interest. In anemia where the hemoglobin is low in amount, its saturation with oxygen may be normal and yet the total amount available for the tissues too little. With poly cythemia, as in congenital heart disease, the saturation with oxygen may be abnormally low and yet the total content—volumes per cent—be sufficient because of the increased number of red corpuscles. Also some oxygen can be carried directly in the blood plasma without attachment to hemoglobin, this is not a large amount but it is of some importance, the ratio of oxygen so carried to that combined with hemoglobin being about 1 to 50

An increase of oxygen saturation of normal arterial blood can be but slight, since it already averages about 95 per cent saturated, but when there is oxygen

unsaturation inhalation of air rich in oxygen (for example, 50 per cent) may restore the blood saturation to normal.

A decrease of oxygen saturation of venous blood below the normal arises first from the various factors already enumerated for decrease of oxygen in the arterial blood. The tissues, in removing their quota, lower the percentage still more, sometimes to a level close to zero in marked stasis. Two important factors are added by the peripheral circulation itself (1) increased tissue metabolism from activity and (2) stasis of the circulation. These may simply be local phenomena, but if they involve enough of the body a very appreciable decrease of oxygen saturation of the venous blood in the right heart will result.

An increase of oxygen saturation of venous blood in the heart above the normal may be found (even up to 94 per cent) when there is a congenital left to right shunt from left atrium to right atrium or from left ventricle to right ventricle or from aorta to pulmonary artery (via patent ductus arteriosus) as determined by cardiac catheterization or when the circulation rate is very rapid and the metabolic activity of the tissues slight, as in paroxysmal tachycardia or it may be found locally when there is rapid circulation which does not give time for the usual oxyhemoglobin dissociation or when there is an arteriovenous aneurysm (anastomosis)

Carbon dioxide in the blood The carbon dioxide content of arterial blood is normally about 60 volumes per cent, i.e., 60 cc of CO_2 gas per 100 cc of blood (26–28 meq per liter milliequivalents per liter = volumes per cent divided by 2.2) The carbon dioxide is carried in the blood chiefly in the form of the dissociated acid sodium salt, whereby the carbon dioxide is quickly taken up and given off. If an excess of other acids appears in the blood stream, as sometimes happens in diabetes or nephritis, the carbonic acid radical is decreased by the blowing off of more than the normal amount of carbon dioxide in the lungs, to maintain the normal blood and body reaction. Or there may be a retention of alkali from the blood to neutralize acid in the body tissue with corresponding decrease in the carbon dioxide content of the blood. In alkalosis the carbon dioxide content of the blood is increased.

A decrease, increase, or normal amount of carbon dioxide may be found in the arterial blood along with an abnormally low oxygen saturation of the arterial blood, though, at first thought, only an increase might be expected. This variability of carbon dioxide content is dependent on the relative influence of three factors (1) reaction of the blood, whether acidotic when in heart failure there is a retention of bicarbonate in the tissues producing a lowered blood carbon dioxide value, or alkalotic, due to excessive vomiting with elimination of acid gastric juice or to excessive intake of alkalies, causing an increased carbon dioxide content in the blood (2) pulmonary overventilation due to oxygen want, resulting in a decrease of arterial blood carbon dioxide, doubtless a factor in keeping this content low in heart disease, and pulmonary underventilation of extreme degree, as in very extensive pulmonary disease resulting in excess of arterial blood CO_2 and (3) a shunt of venous blood into the systemic circulation as in marked congenital heart disease.

sufficient to transmit blood with a high CO content. The product of all these factors determines the carbon dioxide content of the arterial blood. There may be a rise of arterial CO_2 to as high a content as 85 volumes per cent (in a case of extremely marked pulmonary disease—emphysema and purulent bronchiolitis of the left lung with right lung collapsed by hydrothorax—Meakins and Davies, 1925). It may fall to as low as 30 volumes per cent or less from diabetic or uremic acidosis or even from the effect of high altitude (27 volumes per cent in a subject at 14,500 ft elevation—Barcroft and associates, 1922), the normal content averaging about 50 volumes per cent. In heart disease with congestive failure and decreased oxygen content of the arterial blood the carbon dioxide content of the arterial blood is more often decreased than normal or increased. The test of alveolar air carbon dioxide has long been used in estimating the degree of acidosis in disease, but it is not reliable in certain pulmonary conditions, as, for example, when edema of the lungs is present.

A decrease, increase, or normal amount of carbon dioxide in the venous blood may be found as in the arterial blood, but there are two additional variable factors (1) speed of blood flow from arteries to veins and (2) activity of tissue metabolism. If the blood flow is fast or the tissue metabolism decreased, less carbon dioxide is delivered to the blood in the capillaries and the difference between the arterial and venous carbon dioxide content may be reduced from a normal average of about 3 volumes per cent to 1.5 or even 1 per cent; if the reverse occurs, the difference may be increased up to 10 volumes per cent.

Thus, in judging the results of blood gas analysis many things have to be taken into consideration, including accuracy of technic. The data may prove useful in helping to differentiate congenital heart disease with its shunts from acquired heart disease, and in giving actual blood gas measurements for the degree of impairment of the circulation, no matter what the cause. The determination of the blood gases directly or by analysis of the alveolar air also permits an estimation of the blood flow, that is, of the amount of blood pumped by each ventricle per beat and per minute (see page 241).

Blood volume. It is of some importance to distinguish between total blood volume in any given person and circulating blood volume; they are [illegible] means synonymous. It has been calculated that the circulating blood [illegible] in an adult of average size equals 5 to 5½ liters, that is, 3 liters per square meter of body surface or 80 cc per kilogram of body weight (Gibson [illegible] al., 1935). The mean plasma volume measured by Evans blue [illegible] amounts to 45 to 50 cc per kilogram of body weight (Cohen and [illegible], 1948); the volume of the circulating red blood cells has been [illegible] use of radioactive phosphorus (Nylin, 1945) and iron (Dow [illegible] Gibson, et al., 1946) and found to average 30 to 35 gm per kilogram of body weight. Various blood depots will on occasion quite suddenly [illegible] considerable amount of blood from the active circulation to be [illegible] for again by exercise or other requirement. These normal blood [illegible] lungs and systemic veins (especially in the splanchnic region [illegible]

spleen. Abnormal blood depots are most commonly varicose veins of the legs, which may on occasion (chiefly with a change to the standing position) so drain the circulation of blood that faintness or even syncope may occur. Other abnormal blood depots are varicose veins elsewhere than in the legs, lax abdominal vessels, and large hemangiomata. These blood depots are overloaded in congestive heart failure, and the actively circulating volume of blood is also too great, not only for the strength of the heart but in actual amount as well (Gibson, 1941) there may be a real hydremia. In vascular shock the circulating volume of blood is, on the contrary reduced (see Chapter 30)

Available fluid volumes of the human body can be measured by the dilution of sodium thiocyanate injected intravenously The subtraction of the plasma volume and 70 per cent of the red cell volume from the total of the available fluid volume gives the available interstitial fluid volume (Morse, et al. 1947)

EXAMINATION OF THE URINE

Quantity Most important in a patient known or believed to have a failing heart or constrictive pericarditis, acute or chronic, are the determination and interpretation of the quantity of urine excreted compared to the fluid intake. This should be done not for twenty-four-hour periods but for twelve-hour day and night periods for both fluid output and intake in order to note delay in excretion as well as limitation or excess of flow These measurements must be made with a reasonable degree of accuracy and fluid excreted by stool also calculated if the bowel movements are watery We must not forget, however, that normally a considerable loss of water occurs in the expired air and that the sweat glands of the skin excrete water Normally there should always be, therefore, an appreciably larger intake of fluid than output of urine in twenty-four hours, by a few ounces (100 to 200 cc) at least and by a much larger amount where there is much perspiration. Knowledge of the amount of urine alone is of little value, unless this amount is excessively increased or diminished.

If the systemic venous pressure is raised to a high level for a considerable length of time because of congestive heart failure, so that fluid which has been distributed to the tissues at the arterial ends of the capillary loops cannot be wholly reabsorbed at the venous ends, the output of urine is decreased relative to the fluid intake and also delayed beyond the normal. If the osmotic pressure in the capillaries is much decreased because of low serum protein, as in nephrosis and malnutrition, fluid leaves the circulation in too large an amount and the urine output decreases. In either case a decreased urinary output is often a good warning of an impending edema. With the beginning of diuresis the amount of urine increases, and approaches and often surpasses the fluid intake, and edema, if present, begins to subside. It is well to keep a chart of these two measurements routinely day and night in the case of a cardiac patient with congestive failure of any grade at all.

Specific gravity The specific gravity of the urine is of less moment than the quantity but usually varies with it. When the urine output is much decreased in congestive heart failure the specific gravity tends to be high, due to concentration (1 025 to 1 030) but, in spite of a slight to moderate albuminuria, it is not so high as with a like degree of oliguria in health, when the function of normal uncongested kidneys permits full concentration (1 030 to 1.040 or more) When there is a large flow of urine with diuresis, the specific gravity usually varies very little and tends to be low under 1 010 If there is poor renal function, especially in chronic nephritis, the night amount tends to exceed that of the day and the specific gravity usually maintains a fairly constant figure.

The urine concentration test of renal function systematically introduced by Volhard (1918) but simplified by Fishberg (see his fourth edition of *Hypertension and Nephritis* Lea and Febiger Philadelphia, 1939 page 77) is the most practicable of the various functional tests of the kidney for routine use. Briefly it is as follows On the day and night of the test the subject drinks no fluid after the noon meal, eating a dry supper The urine passed during the afternoon and at bedtime is discarded as well as any during the night. The first urine passed in the morning is saved in a bottle. After an hour more in bed a second specimen is passed into another bottle, and still a third after being up and around for an hour without eating or drinking. Fishberg writes

"The specific gravity of each of the three specimens is then taken. If kidney function is unimpaired, the specific gravity of at least one of the specimens will exceed 1.022, often going as high as 1 032. In very severe impairment of renal function the maximum specific gravity is but 1 010 and in intermediary cases figures between these extremes are obtained. In every case exhibiting low specific gravity it is important to observe if edema is being evacuated for this may simulate inability to concentrate. The third specimen passed while the patient is up and about occasionally helps in the detection of orthostatic albuminuria.

Albumin. Albuminuria is an almost constant finding in congestive heart failure· the greater the congestion, the more the albuminuria. In the absence of any trace of edema its presence is far more significant of renal disease, unless it is the slight, inconstant, so-called orthostatic albuminuria or an accompaniment of infection. In the case of subacute bacterial (Streptococcus viridans) endocarditis there is often important renal bleeding and damage albuminuria is therefore a frequent finding in this disease.

Sugar Glycosuria may be transient, slight, and unimportant, it may be of alimentary origin or the result of some accident like cerebral hemorrhage but usually it indicates diabetes mellitus, mild or severe, and then demands particularly conservative treatment in cardiovascular patients (see Chapter 23)

Urinary sediment. Generally when there is congestive albuminuria, red and white blood corpuscles and granular and cellular casts are found in the sediment of the urine. With chronic nephritis hyaline casts are more frequent than in congestive heart failure With subacute bacterial endocarditis, even though

there be no albuminuria, red blood corpuscles are usually found in the sediment. Gross blood in the urine is always important, but is more likely to be due to local infection, stone, or malignancy than to heart disease. Renal infarction secondary to emboli from a diseased heart, in subacute bacterial endocarditis, myocardial infarction with intracardiac thrombosis, or mitral stenosis with atrial fibrillation, is, however an occasional cause of gross hematuria.

Renal function tests. The various tests of renal function, simple or more elaborate, may be applied in the presence of cardiovascular disease but their interpretation must be guarded. The disturbance of renal function may be dependent on either renal disease or secondary congestion from heart failure. The degree of renal impairment as indicated by most of the functional tests is dependent rather on the degree of involvement of the kidneys, whether primary or secondary than on the type of involvement. The combination of both primary and secondary involvement naturally results in the gravest disturbances of function. One must wait until congestive failure subsides before making many deductions from renal function tests. The most practical and useful tests are the urine concentration test, such as that described above under Specific Gravity and the red (phenolsulfonphthalein) test in current use everywhere, emphasizing, however more the rapidity than the amount of the excretion; it is more important to know what percentage of the dye is excreted in the first 15 minutes (normally 25 per cent or more) than in the total time of two hours (60 per cent or more)

CARDIAC OUTPUT MINUTE VOLUME OF BLOOD FLOW AND CIRCULATION RATE STUDIES. PLETHYSMOGRAPHY

Cardiac output. The cardiac output, the minute volume of the blood flow, and the speed of the circulation have been subjects for physiologic investigation for years, chiefly in animals in the experimental laboratory During the last decade the application of such study to clinical medicine has been successfully begun.

Long ago it was shown experimentally that the amount of blood pumped out by either ventricle in the course of a minute, called the *minute volume of blood flow* could be determined readily by a formula (Fick, 1870) based on the amount of oxygen taken up by the lungs in a minute's time and the amount utilized by the tissues. This formula is as follows

$$\text{Minute volume of blood flow (in cubic centimeters)} = \frac{100 \times \text{cubic centimeters oxygen consumed in lungs per minute}}{\text{Difference in volumes per cent between oxygen content of arterial blood and that of venous blood}}$$

The application of this formula to man was for years fraught with difficulties, though the discovery that analysis of the alveolar air permitted a close ap-

proximation to that of the blood gases of the right and left sides of the heart proved very helpful, so that the minute volume of man could be ascertained, and through that the stroke volume or output of each ventricle per beat (by dividing the minute volume by the pulse rate) Another method for determining blood flow was also used, dependent on the absorption of certain gases from the lungs in a certain unit of time, for example nitrous oxide, acetylene, and ethyl iodide acetylene proved to be the most suitable gas for this study (Grollman, 1932) ethyl iodide giving figures 33 per cent too small.

The introduction in recent years of cardiac catheterization has permitted a more accurate determination of the minute volume of blood flow by the use of the Fick formula, since the oxygen content of the mixed venous blood in the right heart chambers can be readily measured and compared with the oxygen content of arterial blood. This volume divided by the pulse rate gives the cardiac output per beat.

Hamilton and his associates (1947 and 1948) have compared the Fick, dye injection, and pressure pulse curves in dog and man in relation to the cardiac stroke volume and have found a fair correlation between the dye injection and Fick findings and a close approximation between dye injection and pulse pressure contour

The application of heart volume changes between systole and diastole as determined roentgenologically has also been suggested recently (Hubacher and Nyffeler 1946) the difference in volume representing directly the stroke volume. The difficulties inherent in measuring the heart volume by x-ray however present a problem here that needs further development (see Chapter 7)

An ingenious but crude, method of determining the output of the heart per beat and per minute was introduced by the use of the *ballistocardiograph* (Starr and Schroeder 1940 Cournand, Ranges, and Riley 1942) This instrument which consists of a delicately balanced table (on which the subject reclines) records the recoil of the body when the blood is ejected into the aorta and pulmonary artery from the ventricles. Attempts have been made to correlate the graphic record which results, called the ballistocardiogram (see Chapter 8) with the output of the heart as determined by the more direct methods noted above, and can apparently with considerable corrections, be used as a rough though inadequate gauge of the cardiac output the latest studies have indicated that the ballistocardiographic index was about one third too low Thus ballistocardiography is best used as a method of study per se and not to determine the cardiac output (see Chapter 8 and Figure 38 page 172)

The minute output at rest normally ranges from 3,500 to 9 000 cc (6 to 12 cc per 100 gm of body weight) being increased by exercise to as high as 25 liters or more in some cases. It may like the stroke volume, be reduced by various factors, but usually to a less degree since an increase of pulse rate tends to compensate for a decreased output per beat. The erect posture has been found usually to cause a decrease (even as much as 30 per cent or more,

but usually less) of the minute volume calculated for the recumbent position. Various other factors influence blood flow in a definite, but sometimes indeterminable, degree these are the stroke volume of the heart, the lung capacity, the absorption power of the lungs, and the capillary diffusion areas of muscles. Physical training makes these factors more favorable and so enables the circulation to be carried on more economically with less strain on heart and arteries, as indicated by less elevation of pulse rate and blood pressure on exertion in the athlete than in the nonathlete. Heart failure is usually attended by a decreased output, but this is very variable and in some cases, as in thyrotoxicosis, the output may still be elevated.

It has been found that the normal output per beat, or stroke volume, varies in the average adult from 50 to 100 cc at rest but that in athletes it may be much higher even 150 cc or more. This is increased by exercise, less in the nonathlete than in the athlete it may be more than doubled, rising for example from 60 to 130 cc or from 70 to 150 cc on vigorous exercise. With heart failure or extreme tachycardia it may be reduced in a case of paroxysmal tachycardia, for example, it has been reported to have dropped from 77 to 13 cc (Barcroft, Bock, and Roughton, 1921)

Circulation rate. In the past the volume of blood flow has been studied more than the rate, but ingenious methods for determining the *rate of blood flow* through important parts of the circulatory system have been devised. A pioneer method consisted of the injection of an active deposit of radium into the vein of one arm and the determination, by means of a detector of the moment of its arrival in the heart and in the artery of the other arm (Blumgart and Yens 1927 Blumgart and Weiss, 1927) The speed of flow from arm vein to heart and through heart and lungs to arm artery was thereby roughly determined. Normally this arm to arm circulation time was found to vary from 14 to 24 seconds (average 18 seconds) a somewhat longer time than has been the finding in the case of more recently introduced substances injected thus time increased with the pulse rate but not with blood pressure variations and was not affected by valvular disease. The circulation rate was *found to be decreased in congestive heart failure according to the degree of failure* and also in atrial fibrillation without failure. Arteriosclerosis and pulmonary emphysema did not cause a delay The arm vein to heart rate of travel of the radium-injected blood showed a wide range of 2 to 14 seconds with an average of 7 seconds in normal individuals.

The recent introduction of the employment of safe radioactive isotopes has revived this earliest method of determining the circulatory rate. Hubbard, et al. (1942) tested the velocity of blood flow in infants and young children using radioactive sodium Prinzmetal, et al. (1949) found the arm to right heart time to average 2 seconds normally in the adult with an *additional* 5 or 6 seconds to the left heart.

Since the earlier days of the clinical application of the study of the rate of the circulation a decade or more ago numerous new methods, consisting mostly of substances for injection into an arm vein, have been introduced.

These have included injections of a dye (brilliant vital red, for example) fluorescein, histamine (which flushes the face) sodium cyanide (causing a sharp increase in respiration) lobeline (causing a deep inspiration followed by a cough) Decholin (sodium dehydrocholate) (giving a bitter taste) glucose or saccharine (detected in the systemic circulation of the tongue by a characteristic taste) aminophyllin, amyl nitrite (lung to face time as determined by a hot sensation) and calcium gluconate and magnesium sulfate (both causing a sensation of heat in pharynx and tongue) to test the rate of the blood flow from the venous side of the systemic circulation through the right heart, lungs, and left heart into the arterial side of the systemic circulation. There is a wide range of sharpness of end point and of practicability among these various substances Hitzig (1947) and Blumgart and Altschule (personal communication) have preferred the use of Decholin with end point at 10 to 16 seconds, which, however has in rare cases caused allergic-like reactions (Norman, 1947) Baer (1940) found calcium gluconate the most desirable in 133 normal persons he found the arm vein to tongue time to range from 8 to 16 5 seconds, averaging 12.3 seconds. He injected 4 cc of 20 per cent calcium gluconate rapidly and then again in 2 or 3 minutes. Papaverine HCl has also been suggested for determining the circulatory rate (Elek and Solarz, 1942) 40 mg (1 25 cc) being the dose recommended, an average of 20 8 seconds (15 4 to 27 0) has been reported between the time of injection and that of the end point, a sudden deep inspiration. In experimental animals acetylcholine has been tried with end point measured by direct inhibitory effect on sinoatrial node (Wilburne et al. 1947)

To test the arm to lung time, that is, the integrity of the venous side of the systemic circulation and the right heart, the injection of ether (Hitzig, 1935) has been most practicable (using 5 minims of ether and 5 minims of normal saline) with end point detected by the subject's consciousness (or even the observer's note) of the presence of ether on the breath. Baer (1940) found the ether arm to lung time in 169 normal individuals to vary from 3 to 9 seconds, averaging 5 8 seconds. Paraldehyde has also been introduced to test the arm to lung time (Caudel, 1938)—the end point is shown by a cough, in 100 adults with normal hearts the range was from 3 to 9.5 seconds, averaging 6 seconds.

Finally the inhalation of CO_2 has been suggested to test the lung to brain time, that is, the integrity of the pulmonary circulation and left heart (Gubner Schnur and Crawford, 1939) acting as a stimulant to the respiratory center its normal range has been found to be 5 to 10 seconds.

Several investigators (Germandt and Nylin, 1946 Meneely and Chesnut, 1947 Nathanson and Elek, 1947) have pointed out the delay in circulation rate that may occur as the result of dilatation of the heart alone even without congestive failure, there remaining a certain amount of residual blood in the heart chambers immediately after their contraction.

The tests of circulatory rate ordinarily employed are the ether time (normal average about 6 seconds) to determine the state of the right ventricle and

Decholin, saccharine, or cyanide time (normal average 12 to 15 seconds) to test the total heart efficiency· the subtraction of the former from the latter gives an estimate of the strength or failure of the left ventricle. The tests are useful in a few cases in which there is some doubt, especially in distinguishing in obscure cases between bronchial and cardiac asthma and in following given patients by serial tests, but they are not routinely necessary

Plethysmography Plethysmography that is, the measurement of volume changes of extremity or organ, has been carried out chiefly in experimental animals, but for certain purposes has been also applied to man It has been used to measure blood pressure to obtain fairly accurate records of the arterial pulse wave, and especially to measure the volume of blood flow in a special part of the body It has little application to routine cardiovascular examination, but in obscure or difficult cases of peripheral vascular disease it may yield information of value. Of late a study of the electrical impedance of an extremity has indicated its possible use in the application of an electrically recording plethysmograph to investigations of the peripheral circulation (Nyboer 1950)

CALCULATION OF THE WORK OF THE HEART AND OF THE *PULSE*

Various attempts have been made to estimate the actual work of the heart and of the pulse some of these have proved of interest, but they have not been of any practical value in cardiovascular examination. We can, for example express by a very rough formula the work of the left ventricle when we know the volume output per beat, the heart rate, and the mean arterial blood pressure. If the left ventricle expels 100 cc of blood per beat at a rate of 60 beats per minute at a mean arterial pressure of 100 mm of mercury (about 1,300 mm of blood) it lifts 6 liters (6 000 cc) of blood to a height of 10 cm of mercury (or about 130 cm of its own weight) per minute, which equals 780 000 gm-cm (or 7 8 kg meters) per minute. The blood vessels maintain this volume at a somewhat lower level through diastole, in addition to withstanding the systolic shock of the heart. This rough calculation expresses in an interesting way the enormous constant activity of the heart. It may further be applied to certain pathologic states for example, if the mean arterial blood pressure is 150 mm of mercury and the heart rate 60 per minute, and the output per beat 100 cc, the work of the heart is 50 per cent greater than in the previous example given, or 11 7 kg-meters per minute. Such a great increase in work, if constant, can explain the hypertrophy of the left ventricle found in hypertension.

It has been calculated (Remington and Hamilton 1947) that the cardiac work performed in maintaining pressure is underestimated up to 1. per cent by multiplying the total ejection by the mean pressure during systole and that the work done by the heart in raising the pressure of the blood is 10 to 40 per cent more than that done at the periphery in forcing blood through the peripheral resistance, energy to this amount being lost as the aortic wave is damped.

More accurate formulas to include still other variables like velocity the effect of gravity and time intervals have been devised, such as the following (Evans, 1918)

Work of heart $= 7\frac{Q \times R}{6} + \frac{W\ (V \times C)}{G \times E}$ where Q equals the quantity of blood ejected, R equals the mean arterial resistance in meters of blood, W equals the weight of the volume ejected, V equals the mean velocity C equals the duration of the cardiac cycle, G equals the acceleration due to gravity and E equals the period of systolic ejection. The complication and incompleteness of such a formula, however renders it impracticable except for experimental animals; moreover it represents not the work of the whole heart but of the left ventricle alone. The need of determining the output of the heart per beat by special methods, the difficulty of ascertaining the mean arterial pressure, the need of cardiac catheterization to estimate accurately the work of the right ventricle because for such calculation the pulmonary blood pressure must be measured in man, and the apparent relative unimportance of the knowledge of the exact amount of work done by the heart have caused the general and probably justifiable neglect of such calculations as these in cardiovascular examination. It is possible, however that more attention paid to the actual work of the heart would be helpful, at least in causing one to realize the great variability that exists not only in disease but also in health.

Calculation of the work of the pulse, as determined, for example, by sphygmobolometry (Sahli) or energometry (Christen) or otherwise, has proved very complicated and of no practical value.

FUNCTIONAL TESTS OF THE HEART AND OF THE CIRCULATION

Strength and endurance tests. Both simple and complicated measures of strength and endurance have been proposed to gauge the health of the heart muscles and of the circulation as a whole. These measures do demonstrate efficiency of the heart along with that of the muscles and nerves, but it is frequently difficult to conclude to what degree abnormal limitation of strength and endurance is due to exhaustion, how much to nervous fatigue, and how much to myocardial weakness. Dyspnea and angina pectoris are the two chief cardiac symptoms of overtaxation of the myocardium and when these symptoms are clearly singly and in a preponderant degree produced by tests of physical activity we may obtain valuable information about the heart. When a sense of exhaustion in local muscles or generally throughout the body or when palpitation, dizziness, and faintness appear with or without dyspnea or heartache (not angina pectoris) other factors then enter in, which prevent carrying the exertion far enough clearly to test the heart strength this is the usual situation, because of the general lack of physical training or because of the ready nervous fatigability in most individuals tested. Hence these tests of strength and endurance generally amount to tests of training and of the nervous

state that is, of physical fitness, rather than of cardiac condition. Neurocirculatory asthenia (or "effort syndrome" or "soldier's heart") and muscular flabbiness are more easily and often exposed by exercise tests than is heart disease. Nevertheless tests of strength and endurance may be applied with some success in estimating myocardial efficiency if sound judgment be shown in the interpretation of the findings.

The simpler the test, the better because a simple test is less likely to strain unaccustomed muscles, less likely to exhaust prematurely a person not in good physical training, and more convenient and practical to execute. In fact such simple exertion as enters into the routine daily life of the patient is best of all. Questioning alone may suffice as to the production of dyspnea or of angina pectoris by climbing a flight or two of stairs at an ordinary rate of speed, climbing a hill of moderate grade at moderate pace walking fairly rapidly on the level, or lifting and carrying a handbag, suitcase, or heavy overcoat. But if there is doubt, or a need for exact data, actual tests of these activities under the observation of the examiner should be executed. Climbing a flight or two of stairs, or if that seems too much, pacing rapidly up and down the room or corridor or mounting and descending repeatedly an especially constructed two-step footstool are perhaps the best of the simple exercise tests. A word of warning should, however be added here, namely that exercise testing in the case of serious coronary insufficiency can prove fatal.

Under some circumstances, as, for example, in examinations for military service, athletic sport or other such activities, more vigorous or special tests are suitable, such as weight lifting, hopping, running, and stepping repeatedly from floor to chair seat and back again Since, however in routine civilian practice one deals often with older men and women or untrained persons with weak or undeveloped muscles, these exercises are not usually applicable. A trained athlete physically fit but with well-marked aortic regurgitation may carry out vigorous exercise tests without any trouble, while an untrained soft-muscled man of the same age, height, and weight with a normal heart may be unable to complete relatively light exercise tests without much fatigue, dyspnea, and palpitation.

The reaction of pulse rate and of blood pressure to exercise has been the subject of considerable study and discussion and has at times been thought to be a suitable test of circulatory efficiency but the same remarks apply to this as to the production of symptoms. Too marked a rise of pulse or blood pressure and too long a duration of this rise after rest begins go with poor physical condition as often as with cardiac weakness alone. Normally after a short spell of exercise of moderate degree (like climbing rapidly two average flights of stairs or lifting during a time interval of one minute two five-pound dumbbells twenty times from the floor first to a standing position and then to an extended position of the arms above the head) the pulse rate and blood pressure in a well-trained young or middle-aged adult should return to normal from elevated levels within two minutes after lying down. The more vigorous the exercise the more slowly do blood pressure and pulse rate return

to resting figures even in the normal subject. The delayed rise of pressure is also of little or no significance normally there is a slight immediate fall when exercise begins before the rise develops.

Over a period of many years various functional tests have been introduced under the names of their respective proposers but thereafter as a rule speedily forgotten. Cabot and Bruce, for example, in 1907 described a group of such tests and imposed a modification of their own. There has, however been in routine use for quite some years, especially in military circles, a certain test for general physical and circulatory efficiency which despite its obvious imperfections has continued to be commonly employed. This is the Schneider Index (1920) It is carried out as follows

1 The patient reclines for five minutes. (a) The heart rate is then counted for twenty seconds. When two consecutive twenty second counts are the same, this is multiplied by 3 and recorded. The score is noted according to Part A, Table 1 (b) The systolic blood pressure is next taken by auscultation two or three readings are made as a check.

2 (a) The patient stands at ease for one or two minutes to allow the pulse to assume a uniform rate. When two consecutive twenty second counts are the same, this is multiplied by 3 and recorded. The score is obtained by the use of Part C, Table 1 The difference between the standing and reclining pulse rate is scored then by use of Part B Table 1 (b) The standing systolic pressure is next taken. The difference between this and the reclining systolic pressure is then scored by Part F Table 1

3 The patient next steps on a chair about 18 inches high, five times in fifteen seconds timed by a watch. To make this test uniform, he stands with one foot on the chair at the count one this foot remains on the chair and is not brought to the floor again until after the count five. At each count he brings the other foot on the chair and at the count down replaces it on the floor This should be timed accurately so that at the fifteen second mark both feet are on the floor (a) Immediately while he stands at ease, the pulse rate is counted for fifteen seconds this is multiplied by 4 and recorded. (b) Counting is continued in fifteen second intervals for two minutes, record being made of the counts at 60, 90 and 120 seconds.

The data from ( ) will be scored by Part D Table 1 taking the difference between this exercise pulse rate and the standing rate. The data in (b) are scored according to Part E, Table 1

The total score is then added up in Parts A, B, C, D E, and F of Table 1 (see next page) The maximum possible is plus 18 and the minimum is minus 11 A score above plus 9 is considered normal a score of 9 or less fails to pass and is reason for a search as to the cause.

A newer test of physical fitness for strenuous exertion superior in its application to athletes and simpler in its execution than the Schneider Index was developed at the Harvard Fatigue Laboratory and is called the Fatigue Laboratory Index (Johnson, Brouha, and Darling, 1942) It is carried out as follows The subject works at a standard hard exercise until he is exhausted,

or if not exhausted, for five minutes. The pulse is counted in recovery fro 1 to 1½, from 2 to 2½ and from 4 to 4½ minutes. The score is calculat from the formula

$$\text{Index of fitness for hard work} = \frac{\text{Duration of exhausting work in seconds} \times 100}{2 \times \text{sum of pulses from } 1\text{–}1\tfrac{1}{2},\ 2\text{–}2\tfrac{1}{2} \text{ and } 4\text{–}4\tfrac{1}{2} \text{ minutes after the end of work}}$$

The larger the score the better the subject, 100 being a very good score. An form of exercise can be used provided it puts sufficient stress on the circula tory system by involving large muscle groups, provided not more than tw

Table 1

POINTS FOR GRADING CARDIOVASCULAR CHANGES IN SCHNEIDER'S TEST OF PHYSICAL FATIGUE AND EFFICIENCY

SCHNEIDER INDEX

A Reclining pulse rate / *B Pulse rate increase on standing (points)*

Rate	*Points*	*0–10 Beats*	*11–18*	*19–26*	*27–34*	*35–4*
50–60	3	3	3	2	1	0
61–70	3	3	2	1	0	1
71–80	2	3	2	0	1	2
81–90	1	2	1	1	2	3
91–100	0	1	0	2	3	3
101–110	1	0	–1	3	3	3

C Standing pulse rate / *D Pulse rate increase immediately after exercise*

Rate	*Points*	*0–10 Beats*	*11–20*	*21–30*	*31–40*	*40–4*
60–70	3	3	3	2	1	0
71–80	3	3	2	1	0	0
81–90	2	3	2	1	0	1
91–100	1	2	1	0	1	–2
101–110	1	1	0	1	2	3
111–120	0	1	1	2	3	3
121–130	0	0	2	–3	3	3
131–140	1	0	3	–3	3	3

E. Return of pulse rate to (standing) normal after exercise

Seconds	*Points*
0–30	3
31–60	2
61–90	1
91–120	0
After 120, two to ten beats above normal	1
After 120, eleven to thirty beats above normal	2

F Systolic pressure standing, compared with reclining

Change in mm	*Points*
Rise of 8 or more	3
Rise of 2–7	2
No rise	1
Fall of 2–5	0
Fall of 6 or more	1

thirds of the subjects can maintain it for five minutes, and provided it does not demand some unusual skill for its successful performance. The only equipment needed is a stopwatch and a means of administering a known amount of exercise at a constant rate Detailed instructions are given for using the test when a treadmill is available.

Respiratory tests. Most of the respiratory tests that have been employed to study circulatory efficiency are restricted in the same way in their clinical application as are the strength tests described above. But here a further complication exists. Diseases of the lungs, pleurae, or respiratory muscles can cause striking reductions in scoring, just as can general weakness, neurocirculatory asthenia, and certain cardiac lesions.

There are various respiratory tests, the most practicable two being that of the vital capacity and that measuring the length of time that the breath can be held. More complicated tests which measure symptom and pulse and blood pressure reactions to certain respiratory efforts, such as maintaining an elevated air pressure in a closed system for a certain length of time or re breathing air in a closed chamber are open to the same objections as those already expressed concerning exercise tests they are tests of physical fitness more than of heart disease or failure also they are affected at times by the additional factor of possible pulmonary disease. Although they may reveal myocardial insufficiency the degree of this must be very carefully interpreted and judged.

Vital capacity The vital capacity of the lungs is the measurement, by spirometer, of the amount of air in liters, that can be expelled by a complete forceful expiration after the fullest possible inspiration. This test was first studied in considerable detail over a century ago (Hutchinson, 1846) Normally the vital capacity varies with the size of the individual, which is best calculated from the surface area, the surface area can in turn be estimated roughly but accurately enough, from the height and weight. The normal ratio averages 2.5 liters of vital capacity per square meter of body surface. A chart has been devised for the determination of surface area (Figure 78B page 143) and tables of average normal vital capacity for male and female American subjects have been constructed. The vital capacity ranges normally from 3 to 4 liters for adult females and from 4 to 5 liters for adult males. It varies somewhat with practice, increasing as a rule on repeated tests until the subject becomes expert. It varies also with physical fitness. An athlete has a higher vital capacity than a nonathlete by as much as 25 per cent or more. Furthermore, the vital capacity is between 5 and 10 per cent higher in the erect than in the recumbent position. In severely exhausted states and in marked neurocirculatory asthenia it may be much reduced, even to 2 liters or less, in an adult who is otherwise healthy with normal heart and lungs. If inexperience, exhaustion, and lack of physical training are excluded as factors, vital capacity reduction means infection, thyrotoxicosis, or pulmonary pleural, mediastinal, or cardiac disease

Vital capacity was originally studied to ascertain the degree of pulmonary

disease, such as phthisis, in which it is usually reduced. Of primary cardiac conditions there are chiefly two that give rise to reductions of vital capacity: mitral stenosis and congestive heart failure. Pulmonary emphysema, no matter what may produce it fundamentally, is also an occasional cause of reduction of the vital capacity. The greater the degree of any of these conditions, cardiac or otherwise, the lower is the vital capacity, especially in the case of heart failure when there may be a reduction to below a liter; such a high degree of reduction does not happen with uncomplicated mitral stenosis. It has been reported that if there is pulmonary edema, breathing dry air may increase the vital capacity as much as 10 per cent or more (Leas, 1927).

The chief value of the vital capacity measurement in the study of a cardiac patient is in following the course of congestive failure. A chart showing the vital capacity at intervals, daily or every few days, is of interest and sometimes of value in such cases, but the test is a crude one and lags behind other evidence of change in the patient as often as it precedes it. It may be concluded that the estimation of vital capacity in cardiovascular examination is not important as a routine measure, except perhaps in pregnancy with heart disease when exertion is by order much restricted and reduction of the vital capacity may be the first indication of impending heart failure. It is not delicate enough to demonstrate very slight grades of cardiac insufficiency and it does not give evidence of organic heart disease in the absence of failure, except in the case of mitral stenosis which acts to decrease the alveolar air by causing engorgement of the lung vessels.

Breath-holding test. A very simple respiratory test, probably as useful as any other and because of its ease of execution the most practicable, is the measurement of the length of time the breath can be held after a full inspiration. All the qualifications with respect to the circulation made above concerning exercise and respiratory tests apply here also. The breath-holding test has one defect, which applies only to certain cases, and that is the possibility of malingering, noted sometimes in soldiers during World War I. It is possible, however, with experience to detect malingering. Practice is sometimes important, as in the case of the vital capacity test. A normal person in good physical and mental condition should be able to hold the breath for more than half a minute, usually about three quarters of a minute and occasionally for over a full minute. Extensive and expert training in underwater swimming and diving may enable an individual to hold his breath as long as two or three minutes or even a bit longer. If the breath cannot be held as long as a half minute the test shows abnormality, consisting of pulmonary or pleural disease, congestive heart failure or lesser grade of cardiac insufficiency, mitral stenosis, general weakness, or neurocirculatory asthenia.

Anoxemia test. The so-called anoxemia test was clinically introduced by Levy and his associates in 1939 to determine the functional capacity of the coronary circulation, especially in persons suspected of having coronary heart disease but without clear-cut angina pectoris or electrocardiographic abnormalities. The test is carried out as follows. The subject breathes a mixture of

10 per cent oxygen and 90 per cent nitrogen for twenty minutes unless cardiac pain is experienced before the end of that time Electrocardiograms (preferably the precordial leads first) are taken routinely just before the test is started and at intervals of five minutes thereafter If the patient complains of discomfort, a record is quickly taken, the low oxygen mixture is shut off, and 100 per cent oxygen administered for one minute

Two hundred and ninety-three of these tests were carried out by Dr Levy and his associates 136 were done on persons apparently free of cardiac diseases and 157 were done on patients with coronary sclerosis. Pain was not induced in any of the normal cases 74 or 47 per cent, of the coronary cases complained of pain, in 54 of which the pain came on during the first 10 minutes. Positive electrocardiographic tests were observed in 77 or 49 per cent. Positivity of the test was considered to be a total *RS-ST* deviation greater than 2.5 mm. Deviation was most marked in Lead 1 and in the precordial leads.

The test has been found useful by Levy and his associates in doubtful cases but has not yet been widely adopted. Some question of its safety has been raised and of the interpretation of slight electrocardiographic variations which might be within the range of normal (Burnett, et al 1942) but in the hands of Levy and his associates (1941 and 1942) and of others since the test has apparently proved both useful and safe. Careful clinical appraisal, however makes rarely necessary either this anoxemia test or exercise tests, though there are always a few individuals in whom the diagnosis may be difficult and for whom such tests are helpful if positive negative tests do not, however rule out serious coronary heart disease with certainty

Tests of the peripheral circulation. Numerous tests of the efficiency of the peripheral circulation have been introduced from time to time. A decade ago a review (Montgomery Naide, and Freeman 1941) summarized their diagnostic importance. The tests have been divided into four groups (A) those which are a part of the physical examination and include observation of local tissue nutrition, color and temperature of skin, palpation of pulse and estimation of blood pressure in different limbs at various levels, rate of blanching on elevation and of flushing and filling of veins on dependency and the reproduction of spasm by immersion of the extremity in cold water (B) tests of capacity of blood flow (vascular function tests) in skin as shown by vasodilatation, by reflex heat, artificial fever anesthesia (local, general, spinal, and paravertebral) intradermal histamine and saline injections, and reactive hyperemia (C) tests of capacity for blood flow (vascular function tests) in muscle, by walking certain distances and by ergographic measurements of muscle fatigue and (D) test of past damage to arteries, by oscillometry and roentgen ray studies, especially by Diodrast injection of arteries or veins. An additional method of study (E) has been more recently introduced consisting of the injection of radioactive isotopes, especially sodium and following its course through any local circulatory area by Geiger counter (Elkin, et al., 1948) As in the case of judgment about the heart by tests, so here, too, much

experience and common sense are needed for proper appraisal in many of the cases.

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PART II

THE SIGNIFICANCE PREVALENCE CAUSES AND TYPES OF HEART DISEASE

CHAPTER 11

THE SOCIAL AND ECONOMIC ASPECTS OF HEART DISEASE

Introduction. The significance of heart disease is far reaching, penetrating and affecting the health and happiness, work and lives, of all peoples on earth and from the cradle to the grave Belatedly the medical profession has at long last taken cognizance of this fact and has begun to enlist the support of patients, social groups, universities, foundations, and finally of local and national governmental resources in the growing struggle to elucidate the causes of heart disease and thereby to clear the way for their control.

Heart disease, or rather cardiovascular disease, has become the chief public health problem of our day Ranking as the leading cause of death it has been widely but crudely publicized, unwarranted fear of heart disease has swept the country in fact all the world. Although it is true that the most recent and most accurate statistics do show a high incidence of cardiovascular deaths, three very important considerations counterbalance in large part the seriousness of such a state of affairs. In the first place, cardiovascular disease, or indeed heart disease itself, is not just one disease but actually a multitude of different diseases, most of which are quite unrelated except as they all involve the heart or blood vessels thus, heart disease is very different from tuberculosis, or typhoid fever or even cancer Secondly the increase in heart disease is in the older age groups, there having been actually a decrease in recent years in heart disease mortality below the age of twenty-five in the United States (Hedley 1939) An old person must *die eventually of some disease process* and a circulatory death is as good to suffer as any indeed probably better than many others. Finally many grades of heart disease of various types are, contrary to old-time tradition, mild and relatively unimportant, compatible with considerable longevity and full activity

However despite these favorable points about heart disease it still leads other diseases as a cause of death from the age of five years to that of twenty it cripples many thousands of young people as the result of congenital defects and of rheumatic involvement of heart muscle and valves, and it strikes down many leaders in professional, business, and political life in middle age at the

height of their careers of usefulness. Thus, there are many aspects of heart disease that concern society and national economy in the home, in the school in industry in the community and in the nation. The present chapter has been newly added to this book in order briefly to discuss these special problems.

Heart disease as it affects the home. Heart disease presents many problems for the home which include the effects both of the chronicity of the condition and of the acute attacks that are so likely to punctuate its course. Thus, in children there are periods of rheumatic fever often very prolonged, which require much patience of the family whether the youngster is in bed at home or away in a hospital or convalescent establishment. Since many times, in the absence of specific therapy these attacks last for months, both child and parents become much depressed and need cheerful medical and nursing care. It has been here that expert social service pioneering and recreational therapy when the state of health permits, have played in late years, an important role. At the Massachusetts General Hospital Miss Edith Terry and Miss Lorena Love have established, under the aegis of the Committee for the Home Care of Children with Heart Disease, the In-Bed Club with its badge and jacket and magazine home visiting schoolteachers and occupational therapy have added their share of aid for these children even before they graduate from bed to rejoin their comrades in the usual life of the community Not only are these patients followed in this encouraging manner while acutely and subacutely ill, but they and their parents are seen at intervals thereafter to help them from acquiring the attitude so common in the past, of resignation to lives of invalidism and fear Often the families need more instruction and building up of morale than do the children themselves. And when much schooling is lost it has been found possible by easygoing and well-controlled summer courses to promote the child to the class ahead along with his mates. In Boston a good additional resource in the care of these children when subacutely ill has been the special foster homes of the Children's Mission when home care proved difficult and hospital attendance impossible or too prolonged.

For the mother ill with heart disease acutely in childbearing age or older or chronically disabled, the choice of an able and understanding housekeeper is not infrequently more important even than nursing care, to relieve both mother and family of undue worry such a person can herself help with the actual nursing too unless the illness is very severe. Another problem concerns the need in some cases of limitation of the size of the family and hence of some method or other of birth control expert advice is here often necessary since the risk of childbirth or even of a needed termination of pregnancy should not be countenanced.

For the father ill with heart disease the threat of disability and death, leaving the family not infrequently inadequately supported, requires much careful planning with expert and friendly advice of doctor and business and professional associates. It often in fact usually is not necessary for the man with heart disease to retire from his life work, except perhaps for a few weeks or

months, even after an acute coronary thrombosis. Years ago it was common practice to advise retirement in such a case, but fortunately we have learned better in the last twenty-five years. Moreover it is wise for a man, young or middle-aged, immersed in his business or professional life to cultivate an avocation or hobby or two not too strenuous, to which he may turn with pleasure if in later life he is prevented by illness, cardiac or of other sort, from continuing his business or professional life, or indeed when he retires simply because of age.

Finally there are the elders of the family grandparents and great-grandparents, who may have heart trouble, the commonest ailment of the aged. They may be a great burden for their juniors, not only medically but socially and financially as well, especially if they perforce reside with them. Much better planning in the future will be needed than in the past to help solve this difficult problem, especially since there will be constantly more and more old people in the world. They themselves must plan better for their future when they are young; their families must acquire a better attitude toward their elders with the respect for age that has been the Chinese tradition and, finally the medical profession and the community itself must devote more time and interest to this problem of the care of old age which has been variously called gerontology and geriatrics, a special field that will one day rank in interest and importance with pediatrics.

Heart disease as it affects the school. The youngest school children, five and six years old, may have heart disease, either congenital or the beginning of rheumatic. In fact these troubles may delay their entrance into school life by a year or more, either because of the severity of the symptoms of the morbus caeruleus or because of active rheumatism which may be severe and prolonged at this early age and require months of bed rest. Except for these two conditions, however most children with heart disease at any age can safely and profitably attend school and need not, in fact should not, be separated off in special categories or classes, except for rare individuals who are unusually crippled by early and marked valvular deformity cardiac arrhythmias, or congenital defects of noncyanotic type. It has not been found necessary to establish, as at one time was planned, special cardiac classes in the public schools. Happily however in many communities home visiting is carried out by public and private schoolteachers when the children are well enough to receive them, thus keeping up both instruction and morale. And when the children do get back to school there is often a sensible arrangement whereby they may be watched and guided without making them overanxious, resentful, or set apart to do this there can wisely be a cooperative plan of schoolteachers, parents, and family doctor.

The instruction itself in the upper classes in the teens can be skillfully directed toward an interest in sedentary occupations later in life if there is much heart trouble but often there is so little wrong (as for example, slight mitral valve deformity or a small ventricular septal defect) that there need be no restrictions whatsoever present or future. The same principles apply to

athletic sports and gymnastic exercises. Infrequently it is necessary to curtail them, but often it is wise to direct a child to baseball in preference to basketball, hockey or football and to short races and jumping in preference to marathon runs, crew races, distance swims, and heavy skiing.

Most important of all in these various considerations is the individual himself No two patients are exactly alike, and so it is vital to decide about every case on its own merits.

Heart disease as it affects industry business, and professional life. In the past there has been much unnecessary fear of heart disease in its relationship to industry but happily a saner attitude is now developing as the result of informing the public at large of the accumulating experience of the medical profession. During the last generation it has become quite evident, in the first place, that the majority of persons with heart disease live a good many years after its onset, in the second place, that the great majority of such long survivors can live useful and contented lives, and, finally that they are with uncommon exceptions benefited *rather than harmed* by work to which they are accustomed, for which they have been trained, and which they enjoy Far too many "cardiac invalids have resulted from the oversolicitous attitude of family friends, or even physicians themselves, and from the apprehension of industries, businesses, and professional associates and clients. A recent survey of opinions of experts of the American Heart Association Committee of the Effect of Strain and Trauma on the Heart and Great Vessels has confirmed the experience of the author in this respect, namely that the routine activity of persons in industry business, and the professions, if carried on in a sensible manner neither initiates heart disease nor makes it worse, if it is already present, unless it is very severe or going through an active stage, as in the case of acute rheumatic carditis, of acute or subacute coronary insufficiency or of myocardial insufficiency Under the conditions of such complications, omission of work and rest at home or in hospital are, of course, indicated, but often only temporarily for after these conditions have cleared up many persons can safely resume work to advantage to both morale and physical health, to say nothing of their economic status in the support of themselves and of their families.

One must, of course, separate off from the routine strains of industry business, and the professions, accidents and trauma, physical or mental, which can occur just as often at home or at play or in the crowded traffic of the present day (see Chapter 23) As a matter of fact, acute coronary thrombosis and deaths from angina pectoris and cerebral vascular accidents are much more likely to occur away from work than on the job, and often even in bed. There should be a clearer understanding by industry and more widespread satisfactory insurance laws to meet the problem of the person with heart disease than have existed in the past. One of the pioneers (Dr Irving Clark) in this regard, who has had experience over many years in the employment of "cardiacs" in industry has emphasized the value and safety of so doing: slowly this word is getting about. Of course, there must be safeguards

such as a careful appraisal of the individual at the beginning, an examination annually or oftener if the need arises, and proper treatment when complications come, as they may whether the person is working or not. Industry should not be blamed for such complications any more than some trivial accident which may have brought to light heart disease which has existed for years. On occasion some unusual strain or trauma may expedite a complication and if so a justifiable and satisfactory attempt can be made to apportion the responsibility of such an exciting factor in the overall picture for example, in a patient with a moderate or considerable degree of mitral stenosis some special strain may set off atrial fibrillation which might not have come on otherwise for some weeks or months or even a year or two, but such strain should not be considered as 100 per cent responsible for the temporary disability that results it may not rate more than 10 per cent.

These remarks apply to every kind of heart disease, even the morbus caeruleus, but, of course, youngsters with severe congenital or rheumatic heart disease should be trained in their youth for sedentary occupations and oldsters may need to reduce their time at work, or sit instead of stand, or shift to another job. With regard to changing occupations one should add that a somewhat active job for which a person is trained, at which he or she is skillful, and which is well liked, may afford actually far less strain than a new job which seems easier physically but which may prove both difficult and boring for the person concerned. Thus, one must individualize advice for every case- lists of occupations for "cardiacs may be somewhat useful but they are only rough guides at best.

We should not deprive our cardiac patients of education or some sort of occupation just because they seem hopelessly handicapped. A good lesson in that respect was taught by a patient of mine with a high degree of the tetralogy of Fallot who, because of much cyanosis and delicate health in early childhood, received no schooling, at the advice of the doctor in attendance because it was thought that such would be a waste of time and money However by good care and good luck he lived to be sixty years old, but, more important still, by sheer will power and genius he educated himself to be one of the leading musical composers of his generation.

Heart disease as it affects the community Much that has been discussed under the headings of home school, industry business, and the professions naturally applies to the community as a whole, but there are other aspects of the community that deserve mention. One is that of the general standard of living. Where there is a low average level, heart disease like a good many other diseases is more common. It is well known, for example, that rheumatic heart disease is twice as common in the poorer more crowded sections of a city than in the suburbs where living conditions are better Much the same statement is true about cardiovascular syphilis, only still more so Also the circulatory diseases of middle age, both peripheral and cardiac are more subject to neglect under poorer conditions of living. We do not as yet, however have an adequate statistical appraisal of their varied incidence, and it

may be that the overnutrition that is more likely to prevail among the well-to-do has its influence in the etiology or at least aggravation of the so-called degenerative diseases such as coronary atherosclerosis and hypertension. A community sense of responsibility for health conditions builds up slowly but eventually leads to the establishment of a proper health agency in close harmony with private practitioners, hospitals, and medical schools. Some small communities in the country today lack physicians close at hand, they should join others in similar plight, or perhaps better situated, to set up some central group or hospital where someone trained in the field of cardiovascular disease can be available, as in other specialties, with essential equipment such as electrocardiograph and fluoroscope.

Heart disease as it affects the nation. Next to last, we come to the problem of the national health. That statistically so far as the heart is concerned, will be dealt with in the next chapter but there are a few additional comments to be made here In the first place, heart and peripheral circulatory diseases are by far the most common causes of death in the U.S.A. today and so naturally they hold the limelight in the current national health program. Fortunately both public enterprise via the new National Heart Institute and National Advisory Heart Council, established by act of Congress in 1948 and private enterprise headed by the American Heart Association, organized in 1924 are working in close harmony in the support of research and teaching in the field of cardiovascular disease. Happily research has the priority for it is evident that the sooner we discover and thereby learn to prevent the underlying causes of heart disease, the sooner we shall rescue our young people and middle-aged population from cardiac invalidism and death, and the less effort, time, and money we shall need to plan for and expend in their care. An increasing mortality from heart disease per se in the years to come need cause no alarm in fact, such may be welcomed provided death comes quickly comfortably and quietly while at rest in bed or easy chair at an advanced age, say at ninety after a long and happy and useful life. But there is still tragedy in the newspaper headlines on occasion when some notable and public-spirited citizen suddenly succumbs to heart disease in the very prime of life and at the top of his career

Heart disease internationally Finally the problem of heart disease is world-wide and what has been said about its community and national relationships applies equally to all nations. An International Cardiac Council was organized in Mexico City in 1946 to help to correlate the various national activities in the cardiovascular field and to aid in setting up the first International Cardiac Congress in Paris in the fall of 1950 At that congress there was established the International Society of Cardiology (Heart and Blood Vessels) There are herein many opportunities for future cooperative researches in the incidence and etiology of heart disease throughout the world and in the strengthening of international medical friendship.

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CHAPTER 12

PREVALENCE OF HEART DISEASE AND OF ITS ETIOLOGIC TYPES

The frequency of heart disease. The first aspect of the prevalence of heart disease to be considered is that of its total frequency though actually this is much less important than a second aspect to be considered later namely that of the relative and absolute frequency of the various kinds of heart disease dependent on the various causes. Accurate information about either the incidence or the prevalence of heart disease in the community is as yet scarcely available anywhere in the world this information is obviously of great importance, and much work remains to be done in securing it. We possess scattered data of small or limited scope or of uncertain reliability from a number of sources, data which are largely incomplete or otherwise unsatisfactory These sources include life insurance statistics, periodic health, school, industrial, athletic, and military examinations, and hospital and mortality figures.

The estimation of community prevalence of heart disease has varied from less than 1 per cent to several per cent. The reported results of examination of school children have differed widely but reasonably satisfactory studies in the northeastern part of the United States have indicated that nearly 1 per cent of children of school age have organic heart disease while in San Francisco only 0 37 per cent of cardiacs were found among the school children, one half or more of whom had congenital heart disease (Sampson, et al., 1938) and in Cincinnati the figure was midway 0.53 per cent, with 55 per cent of them rheumatic and 45 per cent congenital (Rauh, 1939) In 1946–47 Robinson and his associates found among the San Francisco school children 0 44 per cent of cardiacs which, when further analyzed, showed 0.24 per cent rheumatic heart disease and 0 19 per cent congenital heart disease. However rheumatic heart disease was not at all rare among the children of South California some ten to fifteen years ago as indicated by the finding of 3 per cent of cases at autopsy at the Children's Hospital in Los Angeles among patients through 14 years of age. Eighty per cent of the cases at the Children's Hospital were California-born (Thompson, personal communication 1949)

At the Children's Hospital in Boston in 1949 1 3 per cent of the autopsied cases showed rheumatic heart disease and 10 per cent congenital (there were many infants)

The prevalence of heart disease in school children varies very much with climate because of the greater frequency of rheumatic heart disease in cold, wet, and high altitude areas, for example, Sampson et al. (1945) reported 2.04 per cent rheumatic heart disease among the school children of Eureka in the extreme northern end of California in contrast to 0 32 per cent of rheumatic heart disease among the school children in Redlands in the extreme southern end of California. The incidence of congenital heart disease was approximately the same in both places—0 07 per cent in Eureka and 0 08 per cent in Redlands. In 1945 Wedum, et al. reported among school children in Denver 1 63 per cent with rheumatic heart disease

Among 28,139 young adults entering the University of Wisconsin between 1931 and 1939 there were 289 cases (1 + per cent) of heart disease with sex ratio of 1 7 females to 1 male (Cole, 1941) From middle-aged adult examinations and from the certainty that in old age the incidence of heart disease is very much higher than in youth it may be stated as probable that at least per cent of the total population of the northern part of the United States have heart disease of a degree sufficient to produce symptoms or signs.

As a cause of death heart disease has assumed greater and greater proportions in this part of the world until now it leads all other causes, having far outstripped tuberculosis, pneumonia, and malignant disease, the other three most common fatal diseases, and also outnumbering accidental deaths which now rank in third place as a cause of death. This increase which is absolute as well as relative, is due to several reasons, the individual importance of which is not yet known (1) more accurate cardiac diagnosis, (2) fashions and revisions of recording diagnoses (for example, coronary artery disease was classified some years ago under the heading of "arterial disease" in the Massachusetts state records while now it is classified under the heading of "heart disease," most persons formerly diagnosed as having "Bright's disease are now recognized properly as having hypertensive heart disease with congestive failure and not primarily kidney disease and many persons who died of "old age years ago would now be recorded as having died of cardiovascular disease) (3) reduction of incidence of certain other diseases, especially of infections like infantile dysentery tuberculosis, and typhoid fever with a corresponding increasing ratio of heart disease deaths, and (4) actual increase of heart disease, due in part at least to this very same decrease in mortality from other diseases. Some individuals who in former days would have died of dysentery in infancy of diphtheria in childhood, or of tuberculosis or typhoid fever in early adult life now die of rheumatic, syphilitic, hypertensive, or coronary heart disease instead. See Table 2 and Figure 57

[1] It is with much appreciation that I acknowledge the valuable assistance of Mr. Felix E. Moore, Jr., chief of the Biometrics Research Section of the National Heart Institute, Bethesda, Md., in the revision of Table 2 and Figure 57 and for other helpful advice about this chapter

As a background for the increasing mortality from heart disease it is of interest to cite the decreasing death rate in the United States In 1900 the death rate from all causes in the registration states was 1 719 per 100,000 in 1910 it was 1 468 in 1920 it was 1,299 in 1930 it was 1 132 in 1940 it was 1 074 in 1945 it was 1 062 and in 1948 it was 988 The figures for Massachusetts are given in Table 4 It is of much interest that mortality from epidemics has been on the decline in late decades. Except for the one serious

Table 2

MORTALITY STATISTICS FOR MASSACHUSETTS, 1900 TO 1945

(Cases allocated to place of residence since 1935)

Year	Death rate per 100,000 population				Total death rate per 1,000 population	Infant death rate per 1,000 live births
	Diseases of the Heart	Cancer	Tuberculosis (all forms)	Pneumonia (all forms)		
1900	165	75	214	172	18.4	
1905	196	89	192	153	16.7	
1910	200	94	164	175	16.1	
1915	201	103	139	159	14.3	101
1920	215	115	114	156	13.8	91
1925	48	124	83	118	12.4	73
1930	282	136	64	93	11.6	60
1935	336	148	46	89	11.5	48
1940	412	169	38	58	11.8	34
1945	442	187	39	49	12.2	31

Source National Office of Vital Statistics
Not available on comparable basis before 1915

epidemic of influenza at the end of World War I there have been no increases in mortality from epidemic disease since the beginning of the twentieth century (see Figure 58 for Baltimore)

In previous editions of this book it was stated that approximately one out of every three or four deaths in the U.S.A. at large and in individual areas (such as the State of Massachusetts) was due to heart disease, but steadily the proportion has risen, so that now if we include all the ramifications of cardiovascular disease, including, for example, renal vascular disease, the ratio is very close to one out of two (49.5 per cent) Figure 59 illustrates well the recent data.

The accuracy of death certificates is still subject to great improvement but it has gained rapidly during the last generation. That the increasing percentage of cardiac deaths is not a unique feature of this country is shown by statistics recently received from France In Lyons from 1887 to 1891 deaths caused by heart disease made up 7 7 per cent of total deaths from known causes, while from 1938 to 1940 they made up 17.3 per cent, in large part apparently because of the reduction in mortality from other diseases since the actual number of cardiac deaths did not increase proportionately (Paris letter February 7 1942, *J.A.M.A* 1942, CXVIII, 1155) This very increase in

mortality from heart disease provided it comes in old people, may be a source for congratulation rather than dismay since it means that life is now being limited by the degenerative lesions of old age rather than by the infections of youth. But such degenerative lesions should not appear in youth or middle age. The relationship of morbidity and mortality to age is thus a vital one in any consideration of statistics of public health. See Figures 60 and 61 on pages 271 and 272.

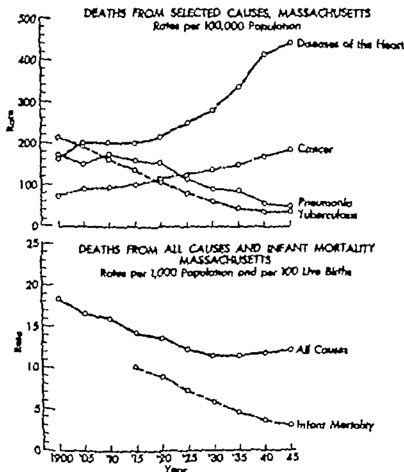


FIG. 57 Death rates from diseases of the heart, cancer, tuberculosis, and pneumonia, and death rate from all causes and infant mortality rate. Massachusetts, 1900–1945

It is of great interest that the average duration of human life has more than doubled in the United States of America in the brief interval since its establishment 165 years ago. It has been estimated that the average duration of life in this country in 1790 was about 30 years. In 1930 it was 58.8 for white men and 62.4 for white women, and in 1947 65.16 for white men and 70.54 for white women. This greater longevity of females has been con-

sistently 4 to 5 years for many decades (Dublin 1933 1941—*Statistical Bull. Metropolitan Life Ins Co* 1949 XXX, No. 10) The expectation of duration of life among the Negroes in the United States in 1930 was 13 years less than that among the whites In 1947 it was reduced to 8 years In 1911 among the policyholders of the Metropolitan Life Insurance Company the expectation of life was 46 6 years and in 1949 less than four decades later it was 67 8 years. In some parts of the world where infant mortality and youthful infections are still high, the average duration of life is still only in the twenties, about as it was probably in Europe in the Roman Era and in

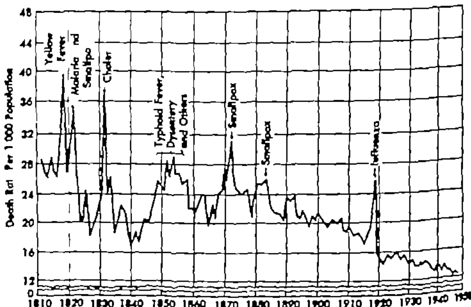


FIG. 8 Annual death rates from all causes with indication of principal epidemics, Baltimore, Maryland, 1812–1948. (Kindness of the Metropolitan Life Insurance Company, New York)

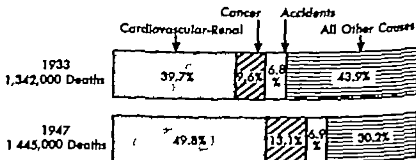


FIG. 59 Proportionate mortality from leading causes of death in the United States of America. 1933 and 1947 showing the increasing death rate from cardiovascular-renal diseases. (Kindness of Mr Felix E. Moore, Jr National Heart Institute, U.S. Public Health Service, Bethesda, Md.)

the Middle Ages (Figure 62) However despite the wonderful increase in the average duration of human life in this country in the past century or so the expectation of life for the man or woman who reaches 60 years is no greater now than it was years ago, and probably a little less this is a very important aspect of the subject that should receive increasing attention in the future. The longest-lived persons (centenarians) are in the main those who with a good family inheritance of longevity have lived physically active lives in rural surroundings.

Other relationships of morbidity and mortality from heart disease of great importance besides absolute and relative frequency and age, are those to

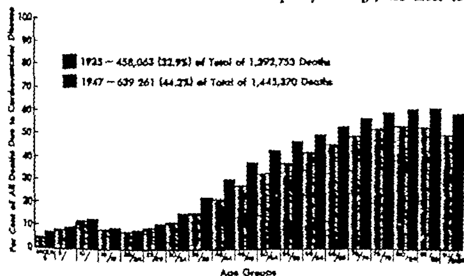


FIG. 60. Chart showing total mortality from cardiovascular diseases as compared to all other causes according to age groups in the United States, 1935 and 1947 (Kindness of Miss Marjorie Bellows, American Heart Association, New York City)

climate, race heredity sex and social and financial status. Favorable influences in reducing the incidence of heart disease in young as well as old, are mild dry climates, good but not rich food, moderate physical exercise, and healthful, uncrowded living conditions Recently it has been noted that a good environment seems to be more important than having long-lived parents in determining the individual's prospect for long life (*Statistical Bull Metropolitan Life Ins Co* February 1942, XXIII, No 2) The importance of heredity in cardiovascular disease however is very great, perhaps as great as, or greater than, any other factor but its exact significance remains obscure. It has also been found that race is sometimes an important factor Negroes showing twice the prevalence of heart disease as do whites. Sex is concerned in three respects in the first place there seems to be a law of nature throughout the entire animal kingdom, from insects up to man, that the male is considerably shorter-lived than the female secondly sex affects the prognosis in every variety of heart disease males living usually a shorter time with any

given heart disease than females probably in part because of the greater burden imposed by the more active life and, thirdly it is related somewhat to the various etiologic types, rheumatic heart disease and heart trouble from thyrotoxicosis being found more often in females, and coronary heart disease and cardiovascular syphilis more often in males The whole problem of the incidence of heart disease needs, however much further study

The causes of heart disease. The second and the most important aspect of

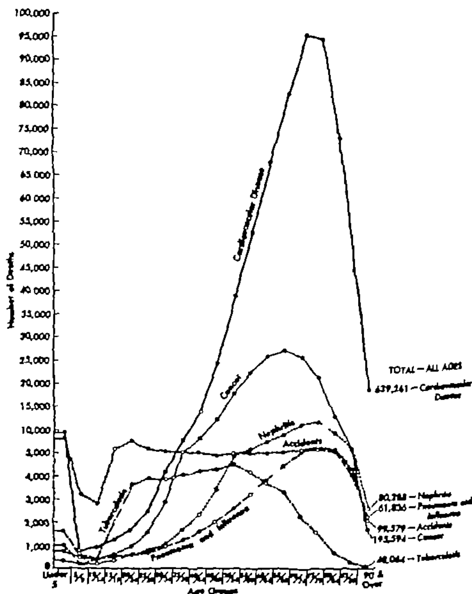


FIG. 61 Chart showing total mortality from cardiovascular disease as compared to all other causes according to age groups in the United States, 1947 (Kindness of Miss Marjorie Bellows, American Heart Association, New York City)

heart disease is that of its causes and their relative frequency With the developing interest in preventive medicine in recent years there has come the realization of the need of analyzing all disease from the etiologic standpoint. Since heart disease is the source of much illness and of high mortality in nearly every community it has attracted much attention, and efforts have been made to determine the relative and absolute importance of various factors thought responsible for heart symptoms and signs. Preliminary classification of causes and etiologic types of heart disease has begun in several communities. It holds much promise for the future, for it is only as we see the importance of etiologic factors of disease that we can view them in due proportion and concentrate our efforts toward the eradication not only of the most

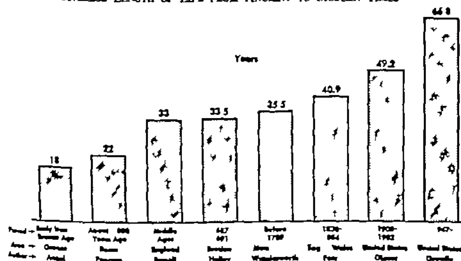


FIG. 62. Chart showing the expectation of life from ancient to modern times (Kindness of Dr Louis I. Dublin, Metropolitan Life Insurance Company New York. Published in *Length of Life*, Ronald Press Company New York, 1949)

serious pathologic states, but also of those most amenable to such an attack in the current state of our knowledge.

It is evident that although investigation of many causes of heart disease may well be carried on at the same time by workers all over the world, the wisest course is to concentrate in any one community on that community's own particular causes most in need of control or most obviously open to attack. In New England the rheumatic infection, hypertension, and presenile coronary disease are the most important factors now demanding study Many years will elapse before we are left with the problem of old age alone. Meanwhile the practitioner of medicine may himself contribute to the progress, either by concentrated study of some particular etiologic factor or factors, or in a routine way by recording as accurately and faithfully as possible in every patient with heart symptoms or signs the causes, whether clear doubtful, or

unknown. Gradually in this way will come a better realization of the problems which lie before the medical profession in this large and important field.

Lest it be thought that the effort of classifying each cardiac patient according to etiologic type is superfluous or an idle fancy of a public health Utopia, I would hasten to add that for the individual patient himself the method is also of great value. Accurate diagnosis, prognosis, and treatment may depend entirely on the recognition of the cause of trouble. It can definitely be said that the etiologic diagnosis is often more important than that of either structural change or functional condition. Congestive failure (myocardial insufficiency) and angina pectoris (coronary insufficiency) are, of course, of prime importance to recognize and treat as functional disorders, but we can handle these cases much more intelligently if we know the fundamental cause of the disease back of their insufficiency. For example, congestive failure complicating coronary occlusion is more serious as a rule than that due to chronic mitral stenosis, and angina pectoris in syphilitic aortitis is more significant than that in rheumatic aortic regurgitation in youth or in mild form in the coronary disease of old age.

There are changing fashions in medical diagnosis. A generation or two ago it was considered sufficient to ascertain the pathologic alterations present in the way of structural damage in the heart, and textbooks were filled with a discussion of valvular lesions and "myocarditis." Then came a step forward when greater emphasis was placed on the functional state of the circulation than had been done before (Mackenzie, 1908). This emphasis was much needed and served an important purpose, but there has been a strong tendency as a result to make too light of the structural defects and indeed hardly to bother to look for them in detail. The pendulum swung too far but there is now fortunately reappearing a growing respect for the lesions in the heart that can themselves serve as sources of strain and failure, or that point to other disease processes or to other sources of strain in the body. We must not think too little of either functional disorders or structural changes; we must seek them all and make note of them, at least those of most importance in cardiovascular diagnosis. A functional disorder like paroxysmal tachycardia sometimes may be alarming but it is usually unimportant and far less significant in diagnosis than is mitral stenosis. On the other hand, a slight chronic rheumatic aortic regurgitation is far less important than is the serious functional disorder of angina pectoris.

It is with the newest element of cardiac diagnosis, the etiologic factor, that this part of the book will deal. This element has long been more or less recognized as of some importance, but only in the last generation has it been emphasized properly (Cabot, 1914). The following quotation represents a milestone in the progress of our study of cardiovascular disease:

Cabot, R. C. "The Four Common Types of Heart Disease. *J.A.M.A.* 1914, LXIII 1461

"To classify cases of disease according to their pathogenic agent or process,

and not solely by naming the region affected or the function disturbed, is the ideal of scientific progress in medicine.

"But until the last decade we have made little advance in this direction as regards the diseases which gravely disturb heart function. Thus we still find in standard textbooks a section devoted to 'mitral regurgitation, its diagnosis, prognosis and treatment, although mitral regurgitation is almost as vague a phrase as 'spinal paralysis' or 'brain fever' Just as a 'spinal paralysis' may be due to trauma, to the tubercle bacillus, to the Spirochaeta pallida, to the organism of poliomyelitis or to cancer so 'mitral regurgitation' is only a symptom caused by the action of streptococci, by the degenerative lesions of arteriosclerosis, by the muscle-tiring resistance of nephritic hypertension and probably by many other causes.

A similar criticism applies to all diagnoses of 'myocarditis.' The micro-organism of rheumatism and of syphilis, the ravages of arterial disease and perhaps many other causes may produce the lesions of chronic fibrous myocarditis, with or without recognizable symptoms. A diagnosis of myocarditis is like a diagnosis of 'ulcer' it calls for an etiologic qualification, such as syphilitic or tuberculous.

"The matter has many practical aspects. A sane prognosis and treatment of aortic regurgitation, for example, depends on knowing or guessing what disease has produced it. Even physical diagnosis may have to await an intelligent interpretation of its results until we make up our minds what micro-organism is at work in the heart, as well as elsewhere in the body

While we should thus emphasize etiology and consider it first and generally foremost, we must not lose sight meanwhile of the other two legs of the tripod of cardiac diagnosis structural change and functional condition. All together the three elements complete satisfactorily our modern idea of analysis of a cardiac case. This represents another step in our progress and a sound one, built upon the experience of the past and of the present. Instead of diagnosing simply mitral stenosis, or atrial fibrillation, or rheumatic heart disease in a given case we should make the complete diagnosis of "rheumatic heart disease (etiologic) with mitral stenosis (structural defect) and atrial fibrillation (disorder of function) (White and Myers, 1921)

Heart disease may be very complicated. Not only are there many different causes of trouble, but two or more of these separate causes may occasion trouble simultaneously in the same heart, and in different and even inconstant degrees. Often much study and discernment are necessary to judge the relative responsibilities of several different causative factors in a given patient, and in some cases it may be impossible to unravel the tangle. In this volume the combinations of etiologic factors that are most common or important will be indicated in the discussion of complications in each chapter.

In the present part of the book the more important causes and etiologic types of heart disease will be given by chapters chiefly according to age prevalence since that is a very practical arrangement, leaving for later consideration certain factors of but slight or doubtful importance or of extreme rarity This plan seems better than that of arrangement according to importance or frequency because it leads one chronologically through the life history of man and because the various factors are of different prevalence and importance in

Table 3—THE RELATIVE PREVALENCE OF THE VARIOUS ETIOLOGIC TYPES

Etiologic Types of Heart Disease		U.S.A. (arranged alphabetically) → Alabama, Welch and Porter 1944, 2,410 cases, 1,400 white, 1,010 Negro. Whites above line, Negro below. 1936–1941.	California (San Francisco) Gager et al 1934. 3,515 cases.	Colorado, Dunlap, 1935, 701 cases among 14,600 hospital admissions (4.8%) in Denver	Illinois, Flaxman, 1934, Cook County Hospital, Chicago 1,646 cases (1913 to 1933), above heavy line, Whites above the line, Negroes below; Miller, Miller and Liberthal, 922 Chicago, 1,000 cases; below heavy line.	Iowa, Myers, 1927. Above line, 510 cases out of total of 1,000 with cardiac symptoms or signs. Fiske and Paul 325 below line, 1,359 cases, University Hospital, Iowa City 1925–1931	Louisiana, Holoubek, Edwards and Baker 1947. 8,313 autopsies, Charity Hospital, 961 heart disease. Whites above line, Negroes below	Minnesota, Clawson, 34 ... 878 cardiac cases among 96,34... autopsies
Congenital anomalies		3.3% / 3.3	5.5%	1.7%	— / 0.6%	2% / 2.6	1.5 / .3	—
Infection	"Rheumatic" type	11.8 / 14.5	22.2	24.8	19.0 / 10.4 / 27.2	30.0 / 27.3	4.7 / 6.36	18.6
	Subacute bacterial endocarditis	0.3 / 0.3	0.9	8.4	3 / 2.1 / 1	— / 1	.86 / .67	11 (Subacute and acute bacterial endocarditis)
	Acute bacterial endocarditis						.32 / .19	
	Cardiovascular syphilis	0.9 / 3.3	7.2	2.6	7.8 / 11.1 / 9.3	3.0 / 2	2.83 / 13.63	7.8
	Others, including diphtheria, tuberculosis, the viruses, and other infestations						1.34 / .36	—
Thyrotoxicosis			2.9	0.5	3.0 / 1.6 / 3	1.5 / .7	— / .4	0.1
Hypertension	Systemic: Hyperplasia	33 / 43.4	31.3	30	33.6 / 48.4 / 26.3	24.3 / 31	2.83 / 28.13	31.3
	Pulmonary: Cor pulmonale	0.9 / 0.7	0.9	0.9	2 / 8.2 / 6		— / .4	1.3
Coronary atherosclerosis (including cases with angina pectoris)		25.8 / 8.7	6 [illegible] included (4)	17.3	21.1 / 6.5 / 24.1	2.8† / 13.47	17.3 / 6.6	25.9
Miscellaneous—Toxic states, trauma, tumors, etc.		3.5 / 6.8		6.4	1.3 / 1.6 / —		1 / 1	—
Unknown		1.0 / 4			2.3 / 0 / —	4.3 / 2	— / .3	—

†Excluding those cases with hypertension.

	New England. *White and Jones*, 1928. 2,431 "organic" cases out of total of 3,000 hospital and private cases with cardiac symptoms or signs. Percentages include both "pure" and "combined" types.	*White.* 9 L. Total of ,000 organic cases 20 years later. Percentages include both uncomplicated and complicated cases.	New York City. *Wyckoff and Lingg*, 1926. 1,00 cases (0 private patients). Public cases above line, private below line.	New York State. *De Porte* 1933. 1,934 cases (seen by 396 physicians).	Ohio. *Scott and Garvin*, 1941. 790 cases who died of heart disease among 6,348 autopsies, Cleveland City Hospital.	Ohio (Cleveland). *Wartman & Hellerstein*, 948, 2,000 consecutive autopsies, 1938–1940. 80% white, 20% Negro. 49.7% cardiac cases.	Oregon. *Cofen*, 1929. 96 autopsied hospital cardiac cases below the line and ,344 private patients with organic heart disease above the line.	Pacific Northwest. *King*, 1935. 356 private patients with organic heart disease.	Rocky Mountain. *Viko*, 1930. 867 "organic" cases out of total of 1,000 with "heart trouble."	Tennessee. *Laws*, 1933. 648 cases of organic heart disease at the Vanderbilt University Hospital, Nashville. White patients above line, Negroes below line.	Texas. *Stone and Vanzant*, 1927. Galveston. 915 cases (501 white, above fine line, 414 Negroes, below fine line); above heavy line. *Schwab and Schulze*, 1931. Galveston. 1,960 cases (whites and Negroes)—ambulatory; below heavy line.	Virginia. *Wood, Jones, and Kimbrough*, 1926. 300 cases (H private patients) including 113 Negroes.	West Virginia. *Condry*, 1932. 18 cases.	Washington, D. C. *Gager and Dunn*, 1933. Above heavy line, 1,200 cases (600 whites above fine line, 600 Negroes below). *Hedley*, 1935. Below heavy line. 480 fatal cases in Washington hospitals in 1932. 288 whites above fine line, 192 Negroes below.
	1.5%	7	0.7%	2.4%			0 %/6%	0%	1 %		1.0%/0.2%	%	0.0%	1.3%/1 %
	39.3 (24% hospital and 39% private)	23	43.8/23	27.2	13	12.8	13/11	28.0	44	15.3/4	8/3/3.4	22	23.7	7.2/4.7/17.1/8.3
	1.9	1			3.5	% nervous disease[illegible]	—/1		0		8/1.2			1.6/1.0/0.4/2.6
	Rare	Rare			7		—/1							
	1	1.0	9.3/3.0	6	3.5		—/4	0		2/13.4	3/31.6/12.7	11	1.6	4.3/12.6/3.0/11.3
	Rare	Rare												
	2.9	0	1		1		—/4	2.0	3		1.2	3½	3	3.7/1.2/0.8/2.1
	39.3	26		30.1	33	27.6	70/26	49.4	14	65.1/71.8 combined ↑	43/30.1/37.2	46	41	3/39.1/43.1/34.3 ↑
		1.1	0		6.8									
	26.7[39]	48.3	"arterio-sclerotic" 18/43.7		23.4		21	30	21.		24/4.3/30.2	46	9.3	36/13.3 combined
	2.1	1.7	trauma		4.7	4	—/3	4			1.4/1.2			
	3	0	1/8.1		3.4		—/8		7.3		3.6/4.1	2		

[39] 39½ per cent of the private patients had angina pectoris and only ½ per cent of the hospital cases

Table 3—Continued

Etiologic Types of Heart Disease		Ill., Am., Bard and Harford, 1939 11,34[illegible] medical admissions, 1,300 cardiac patients	Puerto Rico Suarez, 1943 1937–1944	OTHER COUNTRIES (arranged alphabetically) Argentine Republic Cossio, 1943 20,000 cardiac patients (8,000 hospital; 4,000 private) Buenos Aires	Canada [illegible], 1943 4,300 cases (3,000 hospital, 1,300 private) [illegible]	[illegible], 1943 1,394 cases (1,279 hospital; 115 private) [illegible]	[illegible] ([illegible]) Costa, 1944 438 cases	[illegible] 1948 3,484 patients Institute of Cardiology 1,800 cardiovascular cases
Congenital anomalies		3 7	1.0	2 4	2 5	1 5	1 5	3 61
Infections	Rheumatic type	17 3	17 4	18 2	18 4	23 0	9 3	9 3
	Subacute bacterial endocarditis	13						
	Acute bacterial endocarditis							
	Cardiovascular syphilis	2 3	6.1	7 7	0	0	11 3	15 5
	Others, including diphtheria, tuberculosis, viruses, and other infestations	23						
Thyrotoxicosis		15	7 6	5 0	3	1 2		
Hypertension	Systemic Hypertension	32 2 Hyper & Cor 8	22 8	33 7	20 0	23 0	43 2	23 5
	Pulmonary Cor pulmonale	13		7	1 6	0		
Coronary atherosclerosis (including cases with angina pectoris)		3	39 9	29 6	36 4	39 6	26	31.3
Miscellaneous—toxic states, trauma, tumors, etc.		1 7	10 2	8 9	0 8	2	3	10 0
Unknown		13					4	

By personal communication to Cossio (1943).

Brazil (Cont.) São Paulo. Lambert, et al. 1949 ... patients middle class (above) 4,368 patients "indigent" "lower" (below)	São Paulo. Ramos, et al. 1949 General hospital patients (... cases) (above) private class (2,000 cases) (below)	Ceylon. Gunawardena, 1938 ... cases, including ... from the Colombo General Hospital above line and 400 private patients below line	Colombia. Salcedo-Salgar 1940 323 private patients in Bogotá	Costa Rica. Garcia Carrillo, 1949 3,000 autopsies. Mortality 6 cardiovascular diseases	Ecuador. Carrillo, 1 36 1,000 patients. Hospital cases above line private patients below line	France. Lenègre and Kalondeau, 1949 Paris hospitals specializing in heart disease	India. Vakil, 1949 10,184 medical patients	Mexico. Chávez 1941 1,67 private patients above line and 736 hospital patients below line	Norway. Orjebag, 92 5 cases (... men above line 279 women below line)	South Africa. Hermann and associates, 1939 ... non-European (mostly Kaffirs)	Spain (Madrid) Ortiz-Ferrero, 1949 1950 1,000 cardiac cases (above) 3,000 consecutive autopsies in 2 hospitals (below)	A. Sks. Arneborg, 1917 485 autopsies of 49 countries
	9/15	17/—	2 1	3	2.0%/3.7%	3 8		—/3			2 2/1 3	
13/13	2 6/14 8	30/—	8	3	1 6/13 6	29 2	18	32/41 3	41/37	41 8	28/44 3	21
		21/—	6		—/7 6			6 3/—			3/2 3	
8 6/30 7	14 2/3 6	1/3	7 2	13 3	9/—			8 8/16 9	2 2/4 2	33 3 (many alcoholism)	13 1/8	1
	4/—										—/3 4	
6/10 7	1 1/1 3		3 0		—/3 7			3 0/—			6 8/—	
11 6/14 8	23 7/42 6	13/33	36	23 3	cardio-renal 7 0/8 6	36 8	3	1/3 6		[illegible]	1/—	1
1 7/2 8	3 8/1 3		3 8			5					3 3/6	
19 5/14 1	1/3 3	21+/38+	21	3	senile 6/11 6	12 1 4 with [illegible] patients)	30	23/13 6		14 3	—/1 4	13 0
3/1 2	2/1 3	many with severe [illegible]	13 5	6				6/—			13/9 4	7 4
1/4 6	7/6 3				—/7 6						—	

different parts of the world. In New England, for example, rheumatic heart disease makes up an imposing percentage of all types put together and syphilis as a factor is relatively unimportant, while among the Negroes in the South rheumatic heart disease is far less common and cardiovascular syphilis far more frequent. It is still too early to give satisfactory figures for the prevalence of etiologic types in different parts of the world, only a few studies have been made which allow certain comparisons, and these are not always parallel. The surface has hardly been scratched. A large amount of international cooperative research along these lines deserves early priority

I have tabulated on pages 276 to 279 the etiologic types of heart disease, listed according to age incidence, which may be found helpful as a guide to further study In this list will be found figures of percentage prevalence of the various types reported from New England, New York, Washington, D C, and several states of the South, Middle West, the Rockies, and Far West in the United States, and from England, Norway South Africa, Colombia, Mexico the Argentine, India, and the high seas. The figures are often inadequate and of limited value, but they are the best we possess today slowly they are increasing in number and accuracy (see Table 3 pages 276 to 279)

Finally we must at present leave a space in our classification entitled "of unknown cause thus is still an important group, varying in different localities from about 1 or 2 per cent up to 15 or 20 per cent. This very acknowledgment of our ignorance should act as a spur to us in our studies until eventually we may be able definitely to say "we do know all the causes of heart disease With that knowledge there is bound to come more opportunity to prevent heart disease Incidentally there is an enormous miscellany of diseases which may depress the circulatory function or slightly or terminally alter the heart or the blood vessels (see the end of Chapter 23) but which do not deserve the designation of types of heart disease

To add important and useful information about heart disease in order to help fill the many and serious gaps in our knowledge has required the concentration of many workers in the past three or four decades, especially since World War I (1914–1918) These men and women who have become specialists in this field have advanced our knowledge about cardiovascular disease further in that short interval of time than it had traveled in all the centuries that had gone before, when few doctors had the interest or took the time to study the heart and circulation either in the normal man or in the cardiac patient. This book which is largely a record of the work of the hundreds of students and investigators of cardiovascular disease since 1900 is a testament to that truth.

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CHAPTER 13

CONGENITAL CARDIOVASCULAR DEFECTS

Introduction. Congenital defects of the heart and blood vessels, though not frequent, comprise one of the most difficult, important, and interesting medical problems of our day More progress has been made in our understanding of their clinical significance and in their recognition during the last two decades than in any other type of heart disease the successive editions of this book which were begun just twenty years ago illustrate this well. Also considerable and spectacular advances have been made in the surgical correction and amelioration of several of these defects and intracardiac catheterization has been applied especially in this field. Table 5 (page 294) presents in summary the current clinical status of the congenital defects of the heart and great vessels. Less important, extremely rare, or as yet undiagnosable, defects are not included in this table, but are for the most part mentioned in the listing of 1 000 autopsied cases collected and classified by Maude Abbott. Because of its historic interest and value pathologically her classification and figures have been retained in this edition, but the tabulated insert has been omitted.

Mention need be made herewith only of two rare anomalies incompatible with life, namely acardia (absence of heart) and hemicardia (absence of half the heart) these conditions were reported by Maude Abbott in 15 cases of an early series of hers of 850 autopsied cases (1928)

Incidence. We still await adequate statistical information about the absolute and relative incidence of congenital cardiovascular disease in various parts of the world. Our current impression is that it is found everywhere and in about the same total incidence but that it varies a good deal relatively depending on how much heart disease there is in general and, so far as children are concerned, on how much rheumatic heart disease there is in any district or community Statistics already available, but as a rule still crude, indicate a low total incidence averaging well under 1 per cent of all deaths. An analysis of 34,023 unselected autopsies in Boston showed congenital cardiovascular disease in 1.33 per cent, but this figure dropped to 0.5 per cent after the age of two (Gelfman and Levine, 1942) An incidence of 0 9 per cent of con-

genital heart disease among 15,597 autopsies was reported by Clawson (1944) of this lot of 141 infants, 18 were stillbirths, and 83 died in the first five months of life, only 30 cases (21.3 per cent) surviving after their first year A clinical series of 31 771 medical outpatients in Copenhagen contained 85 cases (0.27 per cent) diagnosed as congenital heart disease among 4 746 individuals with cardiovascular abnormalities (a relative incidence of 1 8 per cent) (Thordarson, 1947) In a clinical series of cardiac patients under the age of twenty years in New England, 6 per cent were found to be of congenital origin (White and Jones, 1928) this figure would doubtless have been higher had more young infants been included since many of those severely involved die very young. In California some years ago (1936) it was noted that the ratio of congenital to rheumatic heart disease was very different from that in New England, being very much greater recent statistical information confirms the earlier figures among San Francisco school children, there being 0 19 per cent with congenital heart disease and 0.24 per cent with rheumatic heart disease, a ratio of about four to five while the ratio in New England was once about one to ten until recent years when with the decrease of rheumatic heart disease and the increase of congenital cardiovascular cases seeking help the ratio has changed in New England to about two congenital to three rheumatic (actually 165 of the former and 257 of the latter under the age of twenty years among 2,000 cardiac patients—White, 1951)

Etiology Cause One of the three great advances in our knowledge of this kind of heart disease during the past decade, not known when the third edition of this book was being prepared, has been the first clear evidence of a causative factor the other two advances being more accurate diagnosis and surgical treatment respectively In the last edition, certain guesses were mentioned, including alcoholism, syphilis, trauma, fetal endocarditis, and defects in the germ plasm, but there was no clear knowledge. It is still quite possible that some of these factors and others not mentioned, or even thought of may prove eventually to play a role, but the one substantiated factor discovered in Australia a few years ago (Gregg, 1941 Swan, 1943) was not mentioned earlier This is German measles (rubella) a virus disease which appears to result in a combination of congenital defects (cataracts, cardiovascular anomalies, and at times deaf-mutism and mental maldevelopment) in a considerable percentage of instances in which the mother is affected during the first two to three months of pregnancy The exact percentage is not yet known, but has been to date estimated to be from one quarter to one half of the cases or even more. One of the most recent reports (Wesselhoeft, 1949) cites 67 infants with congenital heart lesions born of 132 mothers who had had rubella during the first trimester of pregnancy More recently other viruses have been suspected of causing congenital defects of heart and aorta in the fetus during early pregnancy but accurate information about this is still lacking

Our newly acquired knowledge about rubella and congenital heart disease gives us our first real hope about preventative measures. At present the first crude steps have been taken in the way of advice to terminate pregnancy if rubella occurs during the first trimester or to attempt to infect girls and

young women before marriage but, of course, the vital need is early cure and prevention of the viruses themselves. Gamma globulin has been suggested but its value has not been substantiated as yet in the case of rubella.

Not rarely the apparent scarring with fibrosis and contraction of the endocardium of the right ventricle, involving especially the infundibular area and the pulmonary valve itself, strongly suggests the possibility of fetal endocarditis. If this should be proved to be true, we may again have weapons against such involvement in the form of modern chemotherapy and penicillin and its like in fact, it will be of interest to determine whether in the future there may be a decrease in the incidence of infundibular and pulmonary stenosis associated with the current extensive use of these new therapeutic agents during pregnancy On the other hand, the white fibrotic thickening of the endocardium per se, as in the case of congenital anomalies of the coronary arterial circulation (in particular when the left coronary artery arises from the pulmonary artery) is ascribed best to the effect of prolonged anoxia.

Sex There is a curious relationship of sex in certain congenital cardiovascular defects. In the largest series of cases on record (1 000 cases with the sex stated in 859 Abbott, 1931) the ratio of males to females was 58 to 42 It happened that in some of the individual lesions of this series the sexes were about evenly divided, but pericardial defects (21 males to 9 females) cor biloculare, i.e two-chambered heart, and triloculare i.e., three-chambered heart (17 to 10) defects of aortic septum (28 to 11) transposition of arterial trunks (42 to 18) anomalies of the semilunar valve cusps (32 to 5) and coarctation of the aorta (60 to 19) were much commoner in the male, while simple patency of the ductus arteriosus was more common in the female (55 to 29) and in the 53 cases of true atrial septal defect studied by Bedford, Papp, and Parkinson (1941) there was a female preponderance of 4 to 1 more cases, however are needed to allow one to be at all certain of these proportions. Recently the large series of cases of ductus patency operated upon by Gross (personal communication January 1950) gives a ratio of 276 females to 120 males and of coarctation of the aorta by Reifenstein, et al. (1947) gives one of five males to one female.

Age Congenital heart disease may be found at any age but it is commonest of course in the infant and young child because many of the victims survive but a few years at the most, and often only a few days or months. The diagnosis is much more difficult, however in very young children than at an older age, because of the absence or paucity of symptoms and signs this explains why the percentage of accurate clinical diagnoses can be, and often is, higher in general hospitals than in children s or infants hospitals. The age to which the patient lives depends largely on the degree of cyanosis and on the size of the heart; markedly cyanosed children and those with very large hearts rarely survive to adolescence or to full adult age or at most beyond 30 years. Delay in closure of a ductus arteriosus or of a foramen ovale during the first few months of life should not be interpreted as abnormal.

Race Congenital cardiac defects have been reported in every civilized race they do not seek any particular country or climate.

Social status Favorable social status and financial resources have not yet been shown to prevent congenital heart disease but they do favor longevity

Pathology The individual defects found in congenital heart disease will be discussed later in this chapter The most common defects in Abbott s postmortem series of 1 000 cases are interatrial septal defects (373 cases) interventricular septal defects (274 cases) simple patency of the ductus arteriosus (242 cases) pulmonary stenosis (151 cases) anomalies of the cusps of the semilunar valves (146 cases) coarctation of the aorta (adult type) (105 cases) anomalies of the great veins (94 cases) and complete transposition of the arterial trunks (74 cases)

Cases with combined cardiovascular defects are more common than those with the individual defects alone This is particularly true of interatrial septal defects, pulmonary stenosis, interventricular septal defects, and patency of the ductus arteriosus. In Abbott s series of 1 000 cases mentioned above, an atrial septal defect was noted as the primary lesion in but 73 cases, while it complicated other lesions in 300 cases Interventricular septal defects were classified as the primary lesion in 55 cases and as a complication of other lesions in 219 cases, simple patency of the ductus arteriosus occurred primarily in 92 patients and as a complication in 150 others and pulmonary stenosis occurred alone in but 9 cases, while it was combined with other defects in 142 cases. As a matter of fact it is to be expected that the defects should be complicated, either through the simultaneous involvement of several areas of the heart in the embryonic maldevelopment or through the pressure effects secondarily resulting from a single lesion, like pulmonary stenosis, aortic stenosis, or tricuspid atresia (complete closure) to keep patent the ductus arteriosus and defects in the septa between atria and between ventricles. Only in certain instances, as in the case of pericardial defects, of "primary congenital hypertrophy and of coarctation of the aorta, do the defects tend to be isolated rather than in combination.

The stage in the development of the embryo at which retardation or abnormality of growth occurs determines largely the type of congenital heart disease found later If the abnormality comes relatively early before the septa have appeared or have grown appreciably, the heart may remain, as in the case of the primitive vertebrate heart (that of the fish) with but one atrium and one ventricle (cor biloculare) if the defect in growth begins later the heart may be three-chambered, as in the case of the reptile, with two atria and one ventricle (cor triloculare biatriatum) Much less commonly the three-chambered heart has two ventricles and one atrium (cor triloculare biventriculare) [1] Later in the stage of embryonic growth after the septa have almost completely formed, a defect may cause a permanent opening in the interatrial septum (which may be either a patent foramen ovale or a persistent ostium) or an aperture at the base of the interventricular septum just anterior to the "unde-

A unique freak of nature has been reported by Sinclair (1944) of five-chambered heart with two atria, right ventricle, and two left ventricles in t o-headed human monster with tw aortas and t pulmonary arteries.

leaded space." Also at this stage, or earlier the common truncus arteriosus may not be completely divided into aorta and pulmonary artery leaving so-called partial or complete defects of the aortic septum. If in the course of growth of the embryo there is either (1) reversed torsion of the ventricular bend of the embryonic heart, (2) malposition of the aortic septum in relation to the interventricular septum, or (3) incomplete involution of the aortic part of the conus, a transposition of the great vessels may result, the aorta arising from the right ventricle and the pulmonary artery from the left.

In the explanation of transposition of the great vessels in particular Spitzer's important phylogenetic theory deserves a leading position (1923) Harris and Farber (1939) have written about it as follows

"Spitzer's main contribution is a theory of normal cardiac development. The fundamental postulate of that theory is the orderly development of the organ, as a unit, in response to the varying conditions, forces and demands in a series rising from fishes to birds and mammals. It admits of no fortuitous variations which disregard the phylogenetic interrelations of these groups.

"With the advent of pulmonary respiration in phylogeny a very much greater volume of blood must pass through the heart. Bending alone becomes inadequate to compensate for the lengthening tendency and torsion must take place. The original right bend initiates the torsion to the right, and the bulbar laments are thrown into a clockwise spiral. Since the heart is fixed at both ends, detorsion must take place and a counter clockwise spiral must be present at the opposite or venous end.

According to Spitzer this is the most important stage in cardiac development *Without it no advance could tak place with faulty degrees of torsion the most bizarr anomalies result.* The concept of torsion recurs repeatedly through Spitzer's hypothesis, and its importance cannot be underestimated. The septum formation must not only separate the pulmonary and systemic circuits but also cross the circuits so that systemic venous blood enters the pulmonary artery and oxygenated blood passes out through the aorta. A straight septum could only cause the circuits to exist side by side as in cases of complete transposition. Torsion conditions the necessary spiral at the arterial end and thus permits the crossing over of the circuits. In order that the countertorsion may not undo this effect, the countertorsion must take place *peripheral* to the entrance of the pulmonary veins. Furthermore, it is through the torsion that the course of the longitudinal folds, along which the blood flows easily is directed more or less into the current. The forces residing in the blood stream may then work on the folds, stimulate them to grow and cause them to develop into septums.

A failure in development of the conus arteriosus, or perhaps an infection involving it or its valve cusps after it has become differentiated into the infundibulum of the right ventricle, results in pulmonary valve, or oftener infundibular stenosis or atresia. If this stenotic defect comes late it may occur as the only ventricular abnormality but this rarely happens generally it develops early along with failure of the interventricular septum to close completely with diversion of the blood into the aorta from the right ventricle in

a variable but usually considerable degree In most of such cases the aorta is dextroposed, overriding in varying extent the ventricular septal defect and best explained by Spitzer's theory It is this combination of pulmonary stenosis, interventricular septal defect, dextroposition of the aorta, and hypertrophy of the right ventricle that is more commonly found than any other cardiac condition in children (over a year old) and adults with cyanosis resulting from congenital heart disease This is the so-called tetralogy of Fallot, described by Stensen (Steno) in 1672, Sandifort in 1777 Hunter in 1784 Farre in 1814 Gintrac in 1824 and Peacock in 1858 but analyzed more completely as a clinical entity by Fallot in 1888

Fallot, A. "Contribution à l anatomie pathologique de la maladie bleue (cyanose cardiaque) *Marseille méd.* 1888, XXV 77 138 207 270 341 and 403.

Fallot s conclusions are as follows (translation by myself)

1 Clinicians have until now considered the precise diagnosis of the anatomic lesions of congenital heart disease with cyanosis (la maladie bleue) as almost impossible and to be expressed in the form of an entirely vague and uncertain hypothesis. From observations that we have assembled it appears on the contrary that congenital heart disease with cyanosis, above all in adults, is the result of a small number of perfectly definite cardiac malformations.

"2. Of these malformations there is one which in frequency surpasses all others, since we have met it in almost 74 per cent of our observations It is this malformation then that the clinician will be justified in diagnosing and in so doing the chances of error which he will run will be relatively few

3 This malformation constitutes a true pathologic-anatomic type represented by the following tetralogy (1) stenosis of the pulmonary artery (2) interventricular septal defect, (3) deviation of the origin of the aorta to the right and (4) hypertrophy of the right ventricle, almost always concentric in type. At times there is an additional entirely accessory defect namely patency of the foramen ovale.

4 One cannot at the present time attribute the maladie bleue to the persistence of the foramen ovale without direct opposition to the great majority of observed facts; when the communication between the two auricles exists alone without any other associated cardiac lesion, cyanosis does not result.

"5 From the historical point of view one finds, in the writings of the last century (the eighteenth) and of the beginning of the present, frequent observations of congenital heart disease with cyanosis the majority present the interesting combination of the various cardiac lesions mentioned above.

"6. Finally from the pathogenic point of view the theory that considers the interventricular communication as a simple phenomenon belonging to the group of recessive anomalies rests only on a superficial and inexact interpretation of the facts, the incompletely developed septum in the victim of the maladie bleue can be considered in no way as the analogue of the false septum of vertebrate animals with communicating ventricles, it appears much more logical and more in keeping with physiological laws to regard the entire series of cardiac anomalies enumerated above as the consequence of the stenosis of the pulmonary artery As to the cause of this pulmonary stenosis we believe that we should attribute it not to a simple arrest in development, but rather to a pathological process occurring in the region

of the pulmonary valve and of the infundibulum just below it during intrauterine life.

Much rarer than the tetralogy of Fallot is another somewhat similar combination of congenital defects consisting of dextroposition of the aorta (which is quite likely the primary condition, as indeed it may be also in the tetralogy of Fallot) interventricular septal defect, large right ventricle, and normal or increased size, rather than stenosis, of the infundibulum and pulmonary valve and artery (Eisenmenger 1897 Rosedale, 1935) A new entity associated with persistent cyanosis from birth with clinical, fluoroscopic and electrocardiographic findings very similar to Eisenmenger's complex, with which it is likely to be confused, has been recently described by Taussig and Bing (1949) This new entity includes transposition of the aorta and a partial overriding of a ventricular septal defect by the large pulmonary artery arising primarily from the right ventricle.

Finally of the commoner defects, coarctation of the aorta and permanent patency of the ductus arteriosus appear latest of all, at birth or shortly after when the heart and great vessels have otherwise attained normal growth and relations they may then occur alone, probably because they are late defects. Patency of the ductus arteriosus may really be designated as a postnatal defect since normally the ductus does not close until the first few days, weeks, or months after birth, the ductus arteriosus was closed before the age of 8 weeks in 88 per cent of 558 normal infants hearts, and the foramen ovale prior to 12 weeks after birth in 87 per cent of this same group (Christie, 1930) Recently Everett (personal communication, 1951) has found that the foramen ovale closes sooner after birth, considerably before the ductus arteriosus.

Clinical classification of congenital cardiovascular disease. Various attempts have been made to group the different congenital cardiac defects and their combinations in order to produce a useful clinical classification not following necessarily any embryologic or pathologic plan. A classical arrangement is that of the division of the cases into three groups (Abbott, 1924 1928 1936) this arrangement is shown slightly modified in details in the following plan. It may be said that the greater the degree of cyanosis, the more serious is the case.

Table 4

CLASSIFICATION OF CONGENITAL CARDIOVASCULAR DISEASE (ABBOTT)

(Order based on degrees of oxygen-unsaturation and duration of life in 1,000 autopsied cases analyzed by Abbott.)

I. *Cases without Abnormal Communications or Shunt between the Right and Left Sides of the Heart Acyanotic Group* The lesions of these cases cause varying degrees of cardiac strain from little or none to a great deal. Here belong the following relatively unimportant defects as well as more important anomalies

A. Less important group

1 Simple dextrocardia, usually with the situs inversus. No limitation of life unless there are other congenital cardiovascular defects.

2. Anomalies of the pericardium. Defects and diverticula. Maximum age = 75 years, mean age at death in 36 cases = 45 years.

3. Anomalous chordae. Maximum age = 84 years; mean age in 23 cases = 43 years.

4. Uncomplicated quadricuspid and bicuspid semilunar valves, more often aortic than pulmonary: bicuspid aortic valves are a frequent site for bacterial endocarditis and so cannot be considered to be wholly unimportant. Maximum age = 80 years, mean age in 44 cases = 34 years.

5. Double atrioventricular orifices. Maximum age = 71 years, mean age in 9 cases = 37 years.

6. Pure coarctation of the aorta of adult type. Maximum age = 92 years, mean age in 70 cases = 33 years.

7. Anomalies of aorta (such as right aortic arch) of the aortic branches, of the coronary arteries, of the pulmonary arteries, and of the great veins, unless these are extreme. Very variable duration of life, but as high as 87 years with double aortic arch (and as low as 3 months with left coronary artery arising from the pulmonary artery)

B. More serious group

1. Ectopia cordis (extrathoracic heart, in the abdomen) extra-abdominal ectopia cordis does not allow survival for more than a few days. Maximum age = 15 months, mean age in 7 cases = 1 month.

2. Primary congenital hypertrophy" of the heart. Maximum age = 4 years; mean age in 15 cases = 10 months.

3. Pure subaortic or aortic stenosis, which exerts a considerable strain on the left ventricle. Maximum age = 58 years mean age in 23 cases = 13 years.

4. Pure mitral stenosis, very rare. Maximum age = 27 years, mean age in 6 cases = 5½ years.

5. Pure coarctation of the aorta of infantile type, maximum age = 9 months; mean age in 9 cases = 1½ months.

II. *Cases of Arteriovenous Shunt with Possible Terminal or Transient Reversal of Flow (Cyanose Tardive).* In these cases arterial blood ordinarily enters the pulmonary circulation, while venous blood rarely enters the systemic circulation. Potentially cyanotic group

1. Patent ductus arteriosus. Maximum age = 66 years, mean age in 92 cases = 24 years.

2. Localized defects of aortic septum (communication between base of aorta and pulmonary artery or base of right ventricle) Maximum age = 48 years; mean age in 10 cases = 14 years.

3. Localized defects of the interatrial septum, including widely patent foramen ovale, persistent ostium primum, and persistent ostium secundum. Maximum age = 70 years, mean age in 68 cases = 27 years.

4. Localized defects of the interventricular septum Maladie de Roger (Roger 1879) Maximum age = 49 years mean age in 50 cases = 14½ years.

III. *Cases of Venoarterial Shunt (Morbus caeruleus) (Maladie bleue).* Here venous blood in considerable quantity enters the systemic circulation. Cyanotic group

A. Slight to moderate cyanosis

1. Defect of interventricular septum with dextroposition of the aorta. Maximum age = 48 years; mean age in 7 cases = .5 years.

2. Cor triloculare biatriatum. Maximum age = 35 years mean age in 13 cases = 7¼ years.

3. Pulmonary stenosis with patent foramen ovale. Maximum age = 57 years, mean age in 16 cases = 18 years.

4. Tricuspid stenosis. Maximum age = 28 years, mean age in 3 cases = 15 years.

5. Tricuspid atresia (imperforation, from ἀ privative, not, and περαν perforation) with septal defects. Maximum age = 56 years, mean age in 16 cases = 5⅜ years.

B. Moderate to marked cyanosis

1 Pulmonary stenosis with defect of ventricular septum and dextroposition of aorta (tetralogy of Fallot, 1888, the fourth element of the tetralogy being right ventricular hypertrophy) Maximum age = 59 years, 8 months, mean age in 85 cases = 12 years.

2. Pulmonary atresia with defect of ventricular septum, and dextroposition of the aorta. Maximum age = 30 years, mean age in 30 cases = 5 years.

3 Transposition of arterial trunks with defect of ventricular septum. Maximum age = 16 years, mean age in 17 cases = 2¾ years.

C. Extreme cyanosis

1 Cor biloculare with transposition of rterial trunks. Maximum age = 16 years; mean age in cases = 9 years.

2. Persistent truncus arteriosus (complete de ect of aortic septum) with localized defect of interventricular septum. Maximum age = 25 years mean age in 21 cases = 4 years.

3 Cor biloculare with persistent truncus arteriosus (complete defect of cardiac and arterial septa) Maximum age = 14 days; mean age in 5 cases = 6½ days.

4. Complete transposition of arterial trunks without defect of ventricular septum, but with interatrial septal defect or patency of the ductus arteriosus. Maximum age = 11 years; mean age in 3? cases = 6 months.

5. Pulmonary atresia with closed ventricular septum, defective atrial septum, and patent ductus arteriosus. Maximum age = 0 years; mean age in 10 cases = 1½ years.

6. Mitral atresia with aortic aplasia (lack of development, from ἀ privative, not, and λασσειν to form) defect of trial and ventricular septa, and patent ductus arteriosus. Maximum age = 3½ years mean age in 5 cases = 10 months.

7 Aortic atresia, transposition of arterial trunks, closed ventricular septum, patent ductus arteriosus. Maximum age = 15 weeks; mean age in 12 cases = 2 months.

A practical clinical classification which the author has recently found very helpful is presented in Table 5

Symptoms. Congenital heart disease may be present without any symptoms whatsoever if there is no venoarterial shunt or especial strain on the heart such is commonly the case when there is but a slight to moderate d...

Table 5

DIAGNOSABLE CONGENITAL DEFECTS OF HEART AND GREAT VESSELS—1950

			Defect	Symptom	Sign
Intracardiac	Noncyanotic	(a) Without shunt	AORTIC OR SUBAORTIC STENOSIS	O	Grade [illegible] aortic or subaortic systolic murmur and thrill
			2 PULMONARY STENOSIS	O	Grade [illegible] pulmonary systolic murmur and thrill
		(b) With a shunt	3 ATRIAL SEPTAL DEFECT	Slight to moderate chronic dyspnea	Grade [illegible] to [illegible] pulmonary systolic murmur P2++
			VENTRICULAR SEPTAL DEFECT	None with small defects dyspnea with large ones	Grade [illegible] systolic murmur and thrill left sternal border, 4th space
	Cyanotic		5 TETRALOGY OF FALLOT	Retarded growth Easily exhausted Dyspnea Syncopal tendency	Cyanosis and finger clubbing. Grade [illegible] to [illegible] pulmonary systolic murmur
			PULMONARY STENOSIS + ATRIAL SEPTAL DEFECT	Slight to moderate chronic dyspnea	Cyanosis and finger clubbing developing in childhood. Grade [illegible] to [illegible] pulmonary systolic murmur and thrill
			EISENMENGER COMPLEX	Same as for 5, and hemoptysis	Cyanosis and clubbing. May be no murmurs
			TRICUSPID ATRESIA	Same as for 5	Same as for 7
			TRANSPOSITION OF THE GREAT VESSELS	Same as for [illegible]	Deep cyanosis and clubbing. Very large heart. Heart failure
			10 TAUSSIG-BING SYNDROME	Same as for [illegible]	Same as for 7
11 Extracardiac ([illegible])			COARCTATION OF AORTA	O	Hypertension in arms and hypotension in legs. Increased intercostal pulses. [illegible] continuous murmur along spine
			PATENT DUCTUS ARTERIOSUS	O	Continuous pulmonary murmur. Often [illegible] pulse pressure
			VASCULAR RING	Dysphagia Frequent pulmonary infections	

Congenital heart block and coronary anomalies (both very rare) may be diagnosable by electrocardiogram.

*Transposition of aorta and partial overriding of [illegible] ventricular septal defect by the large pulmonary artery arising primarily from the right ventricle.

Table 5—Continued

[illegible] CONGENITAL DEFECTS OF HEART AND GREAT VESSELS—19[illegible]

X-R	ECG	BLOOD	CARD[illegible] C[illegible]	[illegible]
Normal	Normal or Left ventricular hypertrophy	Normal	Normal	0
Pulmonary artery [illegible]	Right ventricular hypertrophy + +	Normal	Pulmonary artery pressure low or [illegible] pressure in right ventricle	[illegible]
[illegible]	R V H + +	Normal	Increased oxygen in right artery. Increased pulmonary artery pressure	[illegible]
Normal as a rule, but with large defects right heart may be enlarged	Usually Normal	Normal	Increased oxygen in right auricle	[illegible]
[illegible]	R V H + +	[illegible]	Catheter obstructed at pulmonary [illegible]	Partial [illegible]
[illegible]	R H + +	[illegible]	The atrial septal defect may be entered by catheter [illegible]	Probably [illegible]
[illegible]	R V H +	Same as [illegible]	Catheter enters either aorta or pulmonary artery. Increased pulmonary pressure	0
Small right ventricle and pulmonary artery	L H	Same as [illegible]	Catheter enters left atrium [illegible] right ventricle	Partial [illegible]
[illegible]	R H Usually	Same as [illegible]	Catheter enters aorta from right ventricle	[illegible] + [illegible]
Large right ventricle [illegible] pulmonary arteries	R H +	Same as [illegible]	Catheter enters aorta from right ventricle. [illegible] pulmonary artery also	[illegible] + [illegible]
Small aorta [illegible]	Normal or hypertensive pattern	Normal	Normal	+
Slightly prominent pulmonary arc	Normal	Normal	Increased oxygen in pulmonary artery. Increased pulmonary pressure [illegible]	+
[illegible] of esophagus and trachea. [illegible] aortic arch	Normal	[illegible]ormal	Normal	+

uncomplicated patency of the ductus arteriosus, coarctation of the aorta, or pure interventricular or interatrial septal defect. On the other hand, there may be marked symptoms if serious congenital cardiovascular lesions are present, especially those attended by marked or extreme cyanosis (Groups III B and III C of Abbott's classification) and those with "primary congenital hypertrophy" marked coarctation of the aorta, or pure stenosis of any of the valves.

The symptom most commonly found is dyspnea particularly on exertion. This dyspnea is of all grades, occurring in the case of atrial septal defects as the result of overloading the pulmonary circulation and thus leaving too little room in the lungs for air and in the morbus caeruleus in paroxysms, due probably to temporary increase of the amount of venous blood shunted into the systemic circulation, which leads in turn to the appearance or increase of cyanosis Often there is but little dyspnea, hardly noticeable, which may show itself simply as an increase in respiratory rate. Dyspnea was noted in 320 of Abbott's series of 1 000 cases of congenital heart disease.

An interesting symptom, doubtless related to both dyspnea and weakness is the frequent squatting, during short walks or other exercise, characteristic of children with the morbus caeruleus, commonly the tetralogy of Fallot.

Along with the higher grades of dyspnea, cough is common hemoptysis is rare but may occur if there is pulmonary vascular engorgement from obstruction, polycythemic congestion, or heart failure. Polycythemia may also give rise on occasion to epistaxis.

Next in frequency after the respiratory and pulmonary symptoms are those of cerebral nature due chiefly to anoxemia, but in the case of considerable polycythemia they are also due to the sluggish circulation and to cerebral thrombosis. Weakness, faintness, headache, dizziness, syncope, convulsions and coma, delirium mania, and transient or persistent paralyses have all been noted, particularly in the cyanotic group of cases with congenital heart disease. The greater the degree of cyanosis, the greater is the likelihood of such cerebral seizures. The cerebral manifestations may last from a few seconds to days at a time they often mean that the patient has been overtaxing his reserve. In some cases they recur at intervals of a few days, weeks, or months for many years. Not rarely they are the cause of death in the cyanotic cases. Paradoxical cerebral embolism in cases with septal defects is responsible on occasion for abscesses of the brain.

Gastrointestinal symptoms in congenital heart disease are not important except for the dysphagia caused by some anomalies of the aorta and its branches, especially a right aortic arch. Faulty circulation to the abdominal viscera may occasion anorexia, nausea, vomiting, hematemesis, tympanites, constipation and combinations labeled "biliousness." If congestive failure supervenes, an increase of such symptoms is common, due especially to engorgement of the liver

Other symptoms are infrequent except for the complaint of coldness of hands and feet with cyanosis, tingling in the extremities, and abnormal susceptibility to infections, especially of respiratory nature. Palpitation is some-

times complained of It is rarely severe Pain is very rare compared to dyspnea.

Signs. Often there are no signs of congenital heart defects outside of the heart, and sometimes there are none even in the heart itself.

Of all general signs only one is both common and important and that is cyanosis, found in slight to marked degree in less than half of the cases of congenital heart disease (noted in 475 cases of Abbott's series of 1,000, doubtless an exaggerated proportion because cyanotic cases attract much more attention than noncyanotic) It may be terminal only due either to a reversal of flow between the sides of the heart through a shunt, or to congestive failure, or to both, it was terminal in 124 of Abbott s series of 475 cyanotic cases. It is particularly likely to be delayed in appearing after birth, but it may become very intense in late childhood and in adult life giving rise to the terms morbus caeruleus and maladie bleue (blue disease) In Chapter 4 cyanosis has already been discussed, here it need only be reiterated that it is dependent on three factors (1) the shunt of venous blood into the systemic circulation, which shunt must be about 30 per cent of the total to pass the threshold for cyanosis, (2) the dilatation of skin and mucous membrane capillaries with peripheral slowing of the blood stream, and (3) insufficient oxygenation of the blood in the lungs. The first two of these three factors are commonly present in the cyanotic group of cases of congenital heart disease, and sometimes the third factor is also added if there is engorgement of pulmonary blood vessels such as occurs in cases of atrial septal defects with overloading of the lesser circulation, or if there is pulmonary arterial and arteriolar sclerosis due to pulmonary hyperemia or hypertension, or with increased viscosity of the blood in polycythemia, or in the rare cases of failure of the left ventricle and of congenital mitral stenosis. A blueness of the eye grounds, cyanosis retinae may be a relatively early sign of the morbus caeruleus.

The next most characteristic and constant sign in the severe cases, that is, in those with well-marked and chronic cyanosis, is clubbing of the fingers and toes (Figure 63) This was noted in 132 of Abbott s series of 1 000 cases. It varies greatly in degree, as does cyanosis, and, like cyanosis, is not frequent in the youngest infants or children It develops later than cyanosis.

Malnutrition and faulty development are not necessary accompaniments of congenital heart disease, even of the severer types, but they have frequently been found. In Abbott's series delayed development was noted 150 times. Faulty cerebral growth, mental retardation, and Mongolian idiocy have been occasionally associated with congenital heart disease. Arachnodactyly consisting of spider-like fingers (and toes) and elongation of the entire body is seen in rare cases of congenital heart disease, and hardly if ever occurs without cardiovascular defects, mostly atrial septal and aortic wall defects.

Edema of lungs and of legs, ascites, and congestion of the liver occur in congenital heart disease only if congestive failure supervenes.

Cardiac examination. Physical examination of the heart yields signs dependent on the type and degree of the congenital defects. There may be little or no evidence of trouble in the heart even in some of the cases with such

serious lesions as the tetralogy of Fallot (pulmonary stenosis, ventricular septal defect, dextroposition of the aorta, and big right ventricle) (Figure 64) There usually is but little enlargement in some cases, however the apex impulse and the left border of dullness are well beyond the midclavicular line, more increased transversely in the fifth intercostal space than downward in the sixth or seventh spaces, since the right ventricle is enlarged more often than the left in congenital heart disease (Figure 71 opposite page 318) There may be increase in dullness to the right of the sternum usually there is not, unless the heart shows well marked general enlargement or an abnormal position (dextrocardia) The region of the great vessels shows no abnormal dullness except with a patent ductus arteriosus or an atrial septal defect when the pulmonary artery may show itself to be enlarged by percussion in the

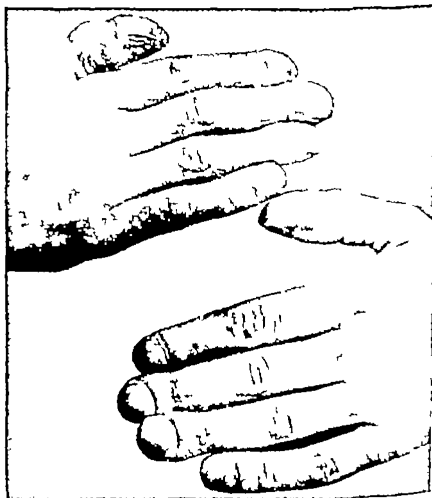


FIG. 63 Photograph showing clubbing of the fingers in the morbus caeruleus (maladie bleue)

second and third intercostal spaces at the left of the sternum. Palpation usually reveals a more or less normal apex impulse. Occasionally there is felt a systolic thrill, located at the left border of the sternum midway between upper and lower ends if there is a pure interventricular septal defect, somewhat higher if there is pulmonary or infundibular stenosis, and maximally in the second right intercostal space if there is congenital subaortic or aortic stenosis. There often is a continuous thrill at the left border of the upper sternum in cases of patent ductus arterious.

Auscultation may reveal no abnormalities, even with serious congenital

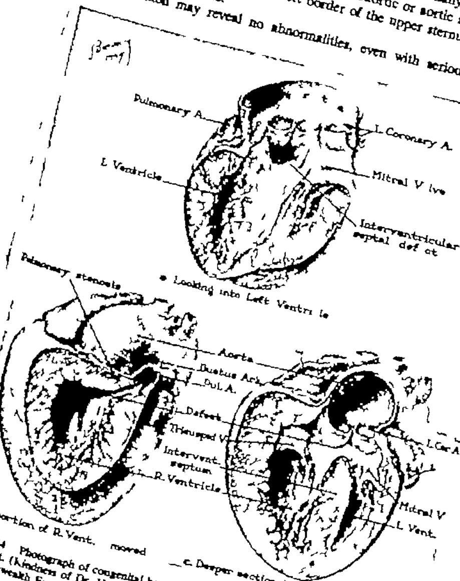


FIG. 64 Photograph of congenital heart showing very large right ventricle in tetralogy of Fallot. (Kindness of Dr Helen Taussig, Johns Hopkins Hospital, Baltimore, and The Commonwealth Fund, New York City.)

defects. There may or may not be murmurs. When murmurs occur they are, as a rule, systolic in time and loudest just to the left of the sternum where they may be very limited in extent, located in the first intercostal space in some cases of patency of the ductus arteriosus, in the second space with pulmonary stenosis, in the third space with infundibular stenosis, and in the third and fourth interspaces in most cases of interventricular septal defect (Roger's murmur) Diastolic murmurs are uncommon as solitary findings, they have been noted where the pulmonary or aortic valve has been defective and in rare cases of patency of the ductus arteriosus or larger interatrial septal defects. They may also accompany the systolic murmurs of dilated pulmonary arteries in cases of large atrial septal defects when they are the result of a stretching of the pulmonary valve rings—such murmurs are likely to be transient like the Graham Steell murmur A continuous murmur roaring and machine-like in character extending throughout systole and diastole, with systolic accentuation, is not infrequently found in the first three intercostal spaces just to the left of the sternum, maximal in the first space. When present it is usually *pathognomonic of patency of the ductus arteriosus if venous hums transmitted from the neck and very rare and obvious arteriovenous aneurysms of the great vessels are excluded, such exclusion is easily accomplished.*

It is important to remember that murmurs and thrills are very variable accompaniments of congenital heart defects the larger the defect, the less likely are murmurs and thrills to be found. A narrow caliber of patent ductus arteriosus or of interventricular septal defect is much more likely to give rise to murmur and thrill than is a large and much more serious patency which may show no murmur or thrill at all. In the case of a stenotic lesion like pulmonary stenosis or coarctation of the aorta the greater the degree of stenosis, the more frequently are murmur and thrill to be found, but here too when the defect is extreme and there is complete atresia, murmur and thrill will be absent. One must use much judgment, therefore, in the analysis of the findings on physical examination of the heart in congenital cardiac disease· it is necessary to depend more on other methods of examination.

Heart sounds, rate, and rhythm are generally not abnormal in cases with congenital cardiovascular defects except in the case of pulmonary stenosis when the second sound in the second left interspace tends to be much diminished while with ductus patency or atrial septal defect it is usually accentuated. With failure the sounds may decrease and the rate may increase, *but marked* disturbances are rare and arrhythmia is very uncommon. Premature beats and paroxysmal tachycardia are seen infrequently Atrial fibrillation is very unusual. There is one disturbance of rhythm, however which is an important, though rare, accompaniment of congenital heart disease this is *heart block*. A few cases of unquestionable congenital heart block are on record. The block may be either partial or complete. It has been thought to be associated with interventricular septal defect and in three cases with postmortem study this defect was found to be extensive in degree (Wilson and Grant, 1926 Yater 1928 and personal communication, Abbott, 1930)

Blood pressure The systolic blood pressure in congenital heart disease is not remarkable. It tends to be low especially where there is an atrial septal defect or subaortic (or aortic) stenosis or much polycythemia and peripheral vasodilatation, then the pulse pressure also is low An interesting finding of a fullness of pulse due to low diastolic pressure is to be noted in some cases of patency of the ductus arteriosus of extensive degree, where a hydrodynamic situation exists somewhat comparable to that in the case of aortic regurgitation. Also it is an important fact for diagnosis that with coarctation of the aorta the blood pressure (systolic and pulse pressure) in the upper extremities is higher than that in the lower extremities, sometimes to a marked degree when the coarctation is extreme.

Roentgenologic study Roentgen ray study of the heart and great vessels in congenital heart disease may be a great aid, but it is sometimes of no help at all, and serious cardiovascular defects may exist with no clear indication of their presence by roentgen ray Positive findings by this method of examination may be, however the only clue to trouble, either to its existence or to the particular lesion or lesions, especially in differentiating left heart involvement from right and in revealing abnormalities of the great vessels. Right ventricular enlargement may be revealed more by the so-called *coeur en sabot* or wooden shoe, shape of heart shadow than by any increase in size of the cardiac silhouette (Figure 72, page 319) this is found especially when the pulmonary artery is hypoplastic (small) as in the tetralogy of Fallot, but not when it is large, even though the right ventricle is very big, as with an atrial septal defect. Marked enlargement of the whole heart shadow is characteristic of congenital idiopathic hypertrophy of coronary anomalies (the left arising from the pulmonary artery) and of von Gierke s glycogen storage disease (see page 323) Undue prominence of the shadow of the pulmonary artery may confirm the diagnosis of patent ductus arteriosus (see Figure 80 page 339) When there is no characteristic murmur of patency of the ductus arteriosus, bulging of the pulmonary arc as seen by roentgen ray strongly favors the diagnosis of a defect in the septum between the atria, and the larger the bulge the more likely is the latter defect. Errors have frequently arisen in the past from relying on roentgenologic rather than on auscultatory evidence of ductus arteriosus patency Marked dilatation of the vessels in the lung hilus shadows helps to establish the diagnosis of an interatrial septal defect (see Figure 68 page 313)

Increase in the shadow of the ascending aorta is especially the rule in the tetralogy of Fallot where the aorta is both dextroposed and abnormally capacious; it may also be found, to a lesser degree, with coarctation of the aorta. Decrease in the ascending aortic shadow is common in the case of atrial septal defects and with aortic stenosis. Absence of the aortic arch shadow may be found if there is considerable coarctation of the aorta, or a right-sided arch may be visible. The esophagus and trachea may be displaced forward by a right-sided aortic arch and compressed by a vascular ring. And finally notching of the ribs may be evident, due to dilated intercostal arteries in cases of coarctation of the aorta (see Figure 77 page 332)

Electrocardiographic examination. In some cases of congenital heart disease the electrocardiogram is normal or so slightly divergent from the normal that it is in no way helpful. Even negative findings are useful however since they tend to rule out right-sided lesions when there is uncomplicated defect of the interventricular septum, patency of the ductus arteriosus, or coarctation of the aorta. There are three conditions where the electrocardiogram is especially helpful and shows characteristic changes. The more common of these three is right ventricular enlargement, usually associated either with pulmonary stenosis, most commonly found in that combination of defects already described as the tetralogy of Fallot, or with interatrial septal defect. These conditions give rise to right ventricular preponderance, often of marked degree. In fact the greatest degree of right ventricular preponderance known is found in congenital heart disease. With this abnormal right axis deviation there is found usually an abnormal increase of amplitude of the *P* (atrial) wave. The second characteristic electrocardiographic pattern is that showing abnormal left axis deviation due to enlargement of the left ventricle in the rare cases of tricuspid atresia here the electrocardiogram may be the chief clue in the differentiation from the tetralogy of Fallot since both conditions cause considerable cyanosis and finger clubbing. The third characteristic electrocardiographic finding is in the case of mirror picture dextrocardia, the so-called heterotaxy (*ἕτερος*, opposite, and *τάξις*, arrangement) whether complete or isolated (that is, with or without abdominal visceral transposition also) here Lead 1 of the electrocardiogram is completely inverted and Leads 2 and 3 are reversed (Figure 65) Isolated congenital dextrocardia, as a matter of fact, has not been found to occur without other more important congenital cardiovascular defects (Roesler 1930) It is of great importance to be certain that this electrocardiogram is caused by the position of the heart and not by artifact due to crossing of the first two lead connections. If as occurs in some cases, dextrocardia is associated with some defect which results in right ventricular enlargement, then the electrocardiogram will indicate a marked degree of abnormal left axis deviation, but with inverted *P* waves in Lead 1 In cases of the two-chambered heart (cor biloculare) or of the three-chambered heart with one ventricle (cor triloculare biatriatum) there tend to be biphasic *QRS* waves of wide amplitude in all three classical limb leads and in the precordial leads. Finally as noted above, there are rare cases of congenital heart block, either complete or partial, requiring electrocardiography for confirmation; it is of interest that the ventricular rate in cases of congenital complete heart block tends to be rather high, in the fifties or sixties, as a rule, and so may obscure the disorder of rhythm until an electrocardiogram is obtained.

Other data Urine Albuminuria is common in the severer types of congenital heart disease, partly because of engorgement due to polycythemia, less often because of slight to moderate congestion from cardiac insufficiency

The blood. Unless there is cyanosis or infection the blood cell counts and hemoglobin will be normal. With a complicating infection polymorphonuclear leukocytosis is of course expected. With cyanosis and a shunt of venous blood

into the systemic circulation a polycythemia is found, increasing in degree as the shunt and cyanosis increase. A red blood cell count of 6 or 7 millions is common in cases classed as the morbus caeruleus and in extreme cases even 10, 11 and 12 million erythrocytes have been reported. Along with this increase of red cells there is an increase of hemoglobin, which usually runs

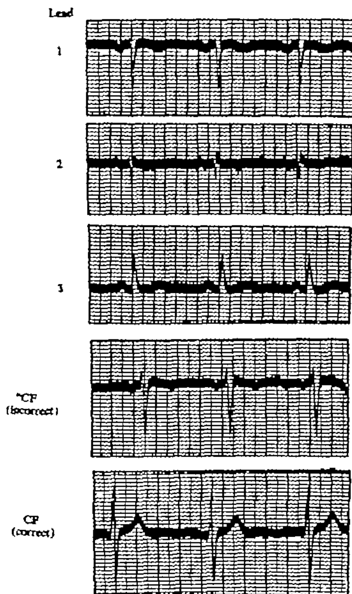


FIG. 65 Electrocardiogram (four leads) in case of congenital dextrocardia with complete situs inversus and without other congenital defects. The first Lead "CF" taken (labeled "incorrect" above) was erroneously obtained from the left side. On discovery of the dextrocardia the correct Lead CF was taken, as shown above. J O male age 30.

parallel, to 110 120 130 and in rare cases up to 180 or 200 per cent (25 gm) The reason for these increases is obvious. Since the oxygen saturation of the hemoglobin is low because of lack of contact of a large percentage of the red cells with oxygen in the alveoli of the lungs, an increase in the number of red cells occurs in order to transport sufficient oxygen to the tissues. The oxygen capacity may almost double while the oxygen saturation of the blood is nearly halved the result is close to a normal amount of oxygen in the blood under favorable circumstances.

The viscosity of the blood is much increased in polycythemia since viscosity is controlled chiefly by the number of cellular elements in the blood. It may be increased several fold. This means more work for the circulation, and peripheral vasodilatation occurs, in part to allow a more complete oxygen distribution to the tissues and in part to relieve the strain on the heart. The actual blood volume is also increased in polycythemia, the amount depending on the degree of cellular increase.

The amount of oxygen and of carbon dioxide in the blood has already been referred to (Chapter 10) It is normal in cases of congenital defects without unusual communications, but there are two abnormal situations dependent on the direction of the shunt, venoarterial and arteriovenous.

Venoarterial shunts. An abnormally low oxygen saturation of the hemoglobin of the arterial blood is common in the case of the defects which result in venoarterial shunts it may reach even the low figure of 58 to 62 per cent (Talbott et al., 1941) If about one third of the venous blood entering the right heart chambers is shunted directly into the systemic circulation the percentage of blue-colored, reduced hemoglobin in the arterial blood may be increased to 20 per cent instead of the normal 1 to 5 per cent (or 4 volumes per cent instead of the normal ½ to 1 volume per cent) passing the threshold at which cyanosis appears. A greater shunt than this yields still more reduced hemoglobin in the arterial blood and a greater degree of cyanosis In the case already referred to with very low oxygen saturation of the arterial blood it was estimated that 75 per cent of the blood in the heart chambers traversed the right to left shunt (Talbott et al 1941) However it is possible for a smaller shunt than that of one third to produce cyanosis, provided there is an abnormally high red cell and hemoglobin content. It is not the percentage but the total amount of reduced hemoglobin, whether originating by shunt in heart or lungs or by peripheral stasis, that is primarily responsible for the abnormal color of the blood, made obvious by dilated capillary vessels. If in the capillaries there are 5 gm or more of reduced hemoglobin per 100 cc of blood, cyanosis will result. With normal red cell and hemoglobin content, 3.5 to 4 volumes of reduced hemoglobin in the arterial blood will yield 6.5 or more volumes per cent in the capillary blood (or 5 gm per 100 cc) With polycythemia and an increased oxygen content capacity of the blood due to increased hemoglobin, the same amount of reduced hemoglobin may be present in the capillary blood to cause cyanosis, even though the actual percentage of oxygen unsaturation of the arterial blood, due to a smaller shunt, may be only 10 or

15 per cent. If it were possible for severe anemia and a very low hemoglobin content (and therefore a low oxygen capacity of the blood) to develop in cases of venoarterial heart shunts, it might be impossible to reach the stage of cyanosis no matter how little the oxygen saturation of the arterial blood might be, because as much as 5 gm of reduced hemoglobin could not be produced in 100 cc of capillary blood. The occurrence of severe anemia in the morbus caeruleus is, however not likely since it would seem to be incompatible with life.

Two other factors often enter into congenital heart disease with a venoarterial shunt to decrease the oxygen content of the capillary blood. One of these is the structural and functional state of the lungs, a factor which, even with cardiac catheterization, makes difficult any accurate estimation of the amount of the shunt. Polycythemia and thickening of the alveolar capillaries are inevitable accompaniments of advanced morbus caeruleus. Failure of proper oxygenation of the blood in the lungs may add its effect to that of a venoarterial shunt in reducing the oxygen content of arterial and capillary blood and in causing cyanosis. The second additional factor consists of the slowing of the peripheral circulation which decreases still further the oxygen content of capillary blood in the morbus caeruleus. The content of oxygen in the venous blood follows that of the arterial blood in such cases, but is several volumes per cent lower An interesting and important factor that helps to decrease the oxygen unsaturation of the blood in cases of right to left shunt is the development of a somewhat compensatory collateral bronchial circulation. The bronchial arteries and their branches course along the bronchi and bronchioles parallel to the pulmonary arteries but with a much more tortuous course. They may become considerably enlarged in cases of the morbus caeruleus, particularly the tetralogy of Fallot, and thus may bring a good deal of blood to the lungs for oxygenation. This bronchial circulation may appear quite clearly in the x-ray pictures of the chest even though the pulmonary artery and its branches are much diminished in such shadows.

The carbon dioxide content of the arterial and venous blood in the morbus caeruleus tends to be low rather than high (as one might at first have expected it to be) This is probably due to increased ventilation whereby the carbon dioxide, which is thirty times more diffusible than oxygen, is pumped out of the blood in the lungs, and also to a tissue acidosis from faulty metabolism (due to the poor circulatory state) with retention of bicarbonate in the tissues.

An interesting effect of venoarterial shunts on tests of the rate of the circulation (see Chapter 10) is worthy of note. In cases with such shunts, in the absence of heart failure, not only is arm vein to tongue arterioles time much reduced below the usual normal because of cutting out the lesser circulation from a good deal of the blood flow but the total round trip ("arm to tongue" or arm vein to leg artery) time may actually be or seem to be slightly faster than the arm to lung time, as in tests with ether

Arteriovenous shunts. The other particular influence of congenital cardiac defects on the blood gases is in the case of arteriovenous shunts, particularly

atrial septal defects patency of the ductus arteriosus, and interventricular septal defects. If large enough, these defects cause, by their admixture of arterial with venous blood, abnormally high oxygen and abnormally low carbon dioxide content of the venous blood entering the pulmonary circulation (Burwell, Eppinger and Gross, 1940 and 1941)

Cardiac catheterization. Catheterization of the heart chambers and pulmonary artery has been discussed in Chapter 10 but one should add here that perhaps its most useful application is in the diagnosis of congenital defects; a higher blood content of oxygen than normal is found in the right atrium in the case of an atrial septal defect, in the right ventricle in the case of a ventricular septal defect, and in the pulmonary artery in the presence of a patent ductus arteriosus. Moreover the catheter can be passed under fluoroscopy through an atrial septal opening into the left atrium or into the aorta in the tetralogy of Fallot (see Figure 56 pages 228 and 229)

Course and prognosis. The course and prognosis of congenital heart disease vary with the type. In cases with relatively unimportant lesions where there are no shunts, for example, abnormal chordae tendineae and valve cusps, simple dextrocardia, pericardial anomalies, slight to moderate coarctation of the aorta, and in cases with lesser degrees of arteriovenous shunt through uncomplicated patent ductus arteriosus or interventricular septal defect, life may not be handicapped or shortened, and with all these conditions old age has been comfortably reached with no cardiac disability due to these defects. Even these lesions are, however somewhat perilous, because of the possibility of their being the site of bacterial infection, especially of streptococcal nature. This infectious invasion, serious and in former days so often fatal, is not rare, particularly in the case of bicuspid aortic valves, of ventricular septal defects, and of patent ductus arteriosus in Maude Abbott's series 9 of 32 cases (28 per cent) of the first named, 13 of 50 cases (26 per cent) of the second, and 21 of 92 cases (23 per cent) of the last-named developed subacute bacterial endocarditis or endarteritis. Gelfman and Levine (1942) found the incidence of acute and subacute bacterial invasion in patients over the age of two years with the more common congenital cardiovascular defects as follows ventricular septal defects (Roger's disease) 57 1 per cent of 14 cases, patent ductus arteriosus 28 6 per cent of 14 cases, pulmonic stenosis 29 4 per cent of 17 cases, bicuspid aortic valves 21 2 per cent of 52 cases, tetralogy of Fallot 28 6 per cent of 7 cases coarctation of the aorta 10 per cent of 10 cases, and *atrial septal defects none among 45 cases.*

In the case of the more serious defects the course is difficult and the prognosis grave. Both the difficulty of the course and the seriousness of the prognosis depend on two factors. The first of these factors is the degree of anoxemia, which is indicated to a certain extent by the degree of cyanosis. This anoxemia affects all organs of the body especially the brain and the heart. The second factor is the amount of direct strain on the heart. Two other points are to be remembered. Cyanosis does not usually appear early in infancy and yet the prognosis at this early age may be bad. Moreover anoxemia

and cyanosis are not strictly comparable, since there may be a sufficient quantity of oxygen in the blood for the tissues if there is a polycythemia and yet there may be also enough reduced hemoglobin to cause cyanosis. This explains why many cyanotic individuals are not dyspneic.

The most serious lesions, like ectopia cordis abdominalis, uncomplicated transposition of the great vessels, the two-chambered heart, and pulmonary or aortic atresia with closed ventricular septum may be so crippling that a miserable existence is possible for but a few days, weeks, or months at best.

Sudden unexpected death is not a rare termination in the case of infants and children with congenital heart disease, even in those who show little or no evidence of the condition during life (Levinson, 1941)

The less grave cases of the morbus caeruleus may occasionally survive to adult life or even into middle age, if they live carefully and are fortunate enough to escape serious complications. Some striking cases are on record of long survival, especially one of a noted musician who lived a useful life to the age of 59 years and 8 months in spite of the tetralogy of Fallot and another of a woman with marked pulmonary valve stenosis and atrial septal defect who lived actively until she died of right heart failure at the age of 74 years and 11 months. Both diagnoses were confirmed by postmortem examination and both patients showed cyanosis and clubbing of the fingers from early childhood (White and Sprague, 1929 White, Hurst, and Fennel, 1950) Limitation of activity is almost always enforced by the morbus caeruleus, because of dyspnea, weakness, and cerebral symptoms.

Complications. The chief complications of congenital heart disease are infections, especially pneumonia, cerebral attacks—syncope, coma, convulsions, and hemiplegia due to thrombosis or hemorrhage—bacterial endocarditis or endarteritis, and *congestive heart failure. These complications are often fatal.* An analysis of 453 autopsied cases of all ages of congenital heart disease in Boston hospitals gave a total incidence of 6 6 per cent affected by subacute bacterial endocarditis or endarteritis as compared with 16 6 per cent among those over the age of 2 years (Gelfman and Levine, 1942) This dread disease is now fortunately in major part preventable or curable because of the advance in surgical therapy and of the introduction of penicillin. An uncommon complication in cases with septal defects is cerebral infarction or abscess from paradoxical embolism

Treatment. In the first two editions of this book (1931 and 1937) it was stated that "there is no curative treatment, surgical or medical, for congenital cardiac defects, but notable advances have been made in the last twelve years in several particulars (1) patency of the ductus arteriosus is now curable by surgery (2) coarctation of the aorta can also be corrected surgically in nearly all young cases, (3) a *vascular ring constricting trachea and esophagus* can be broken, (4) certain instances of the morbus caeruleus, in particular the tetralogy of Fallot, can be greatly helped by surgery and (5) penicillin can cure many of the cases infected by the alpha hemolytic streptococcus. And other advances are in the offing.

In some cases of congenital heart disease no special care is needed, though even the least serious case should be protected against infection, to avoid complicating bacterial invasion and pneumonia. Since the teeth and gums harbor in particular the alpha hemolytic streptococcus, the cause of subacute bacterial endocarditis and endarteritis in the vast majority of cases, it is wise to protect by penicillin the patients with congenital cardiovascular defects who are to be subjected to dental extractions or other extensive treatment; 300,000 units should be given intramuscularly 1 hour before the dental treatment and again 3 hours after

Tonsillectomy is probably advisable in childhood, though not in infancy provided the tonsils are diseased and provided there is not too great a risk for operation. Protection from fatigue and care to provide suitable diet are to be urged for the cyanotic cases and for those with much heart strain. Finally complications of congestive failure, cerebral lesions, and infections are to be treated as such, by rest in bed, digitalis as required, penicillin, and other measures. If the victim of congenital heart disease is well protected his *life may sometimes be prolonged for many years.*

Differential diagnosis. Congenital heart disease may resemble two other conditions, acquired heart disease and pulmonary disease. It is to be differentiated from the former by the history of involvement of the heart from birth, if that is reliably obtained, and by the characteristic signs—certain murmurs, heart shape, cyanosis, clubbing of the fingers, and typical electrocardiograms when such exist (as described above) in a few instances the differentiation is very difficult. Acquired heart disease especially rheumatic, subacute bacterial, and coronary may be superimposed on congenital cardiovascular defects.

It is more difficult to differentiate pulmonary disease, such as pulmonary fibrosis with emphysema or pulmonary endarteritis, when it is attended by cyanosis, polycythemia, and clubbing of the fingers, from the morbus caeruleus of congenital heart disease, especially if the latter happens not to show characteristic murmurs, electrocardiograms, or orthodiagrams. Great care must be taken in analyzing such cases.

The discovery of congenital anomalies elsewhere in the body favors somewhat the diagnosis of congenital cardiovascular defects when the differentiation of the type of heart disease is difficult or obscure.

The more common individual congenital cardiovascular defects should in the present day and age (in striking contrast to a generation ago) usually be differentiated with ease, except in infancy It seems likely that the ratio of diagnosability of individual defects during infancy to that after infancy is about 30 per cent as compared to 90 per cent. Rare defects are, however as a rule undiagnosable

INDIVIDUAL CONGENITAL CARDIOVASCULAR DEFECTS

It has become possible during the present generation clinically to recognize the majority of congenital cardiovascular defects and therefore they have

assumed an increasing importance in the practice of medicine. They will be presented in the following order congenital malposition of the heart, congenital abnormalities of the cardiac chambers and septal defects, congenital myocardial disease, congenital endocarditis and valvular defects, congenital pericardial defects, congenital anomalies of the great arteries and veins, and congenital anomalies of the coronary arteries.

CONGENITAL MALPOSITION

Congenital malposition of the heart includes dextrocardia and ectopia cordis.

Congenital dextrocardia is of two main types occurring with about equal frequency (1) In the first type, without transposition, the heart is slightly rotated and rests in the right side of the chest. The left chambers lie to the left and anteriorly the right chambers lie to the right and posteriorly and the apex is made up either of the right ventricle or of the right side of the common ventricle. Almost invariably in this type there is some serious associated congenital anomaly like a single ventricle. The prognosis and course of the congenital heart disease depend on these associated anomalies and not on the dextrocardia. (2) The other variety of congenital dextrocardia is that attended by transposition of the chambers, whereby the "left" chambers lie on the right side and form the right border and apex and the "right" chambers lie on the left side. Almost invariably the abdominal viscera are also transposed (complete heterotaxy or situs inversus) With this type of congenital dextrocardia, that is, the "mirror type," there are usually no other congenital cardiac defects, at least of serious nature, unless the dextrocardia is isolated, that is, occurring without associated general transposition of other organs (Roesler 1930) Dextrocardia uncomplicated by other cardiovascular defects is unimportant clinically It is discovered accidentally on routine physical or roentgen ray examination, or even by electrocardiography and in no way affects activity or duration of life. A pathognomonic sign of this mirror type of congenital dextrocardia is electrocardiographic complete inversion of Leads 1 and aVR and transposition of Leads 2 and 3 aVL and aVF and of the precordial leads (Figure 65) An interesting complication of the situs inversus, which may in some cases be regarded as a stigma of an associated congenital maldevelopment, is bronchiectasis, which was found in 5 of the 23 cases of the situs inversus (21 7 per cent) recorded at the Massachusetts General Hospital in the fifty years from 1886 to 1936 while of the general hospital population over that period of time bronchiectasis was diagnosed in but 0.3 per cent (Churchill and Adams, 1937)

Ectopia cordis, a very rare defect, consists of the malposition of the heart outside of the thoracic cage either in the abdomen or actually projecting outside the body wall. It is of academic interest only since attempts at surgical correction have as yet been unsuccessful and life is almost invariably very brief a matter of a few days or at best a few weeks.

CONGENITAL ABNORMALITIES OF CARDIAC CHAMBERS. SEPTAL DEFECTS

Congenital abnormalities of the cardiac chambers include complete and partial absence of atrial and ventricular septa.[2] These defects may be unimportant, discovered only at postmortem examination after a long and active life and unsuspected before death, or they may be of great importance, permitting only a few hours or days of existence after birth. The degree of the defect and complicating abnormalities determine the importance of each lesion.

Atrial Septal Defects

Atrial septal defects are much more numerous than any other anomaly in congenital cardiovascular disease. In Abbott's series of 1,000 cases there were 402 individuals with openings between the atria, which included true (*not slit-like*) *patency of the foramen ovale* (290 cases), persistent ostium primum in the lower part of the septum (36 cases), persistent ostium secundum in the upper part (19 cases), multiple defects (28 cases), and complete absence of the septum in the biloculate heart (14 cases) or in the triloculate heart with one atrium and two ventricles (15 cases).

Patency of the foramen ovale is of the least importance and greatest frequency of all congenital cardiac abnormalities. The foramen ovale is a valve-like opening between the atria developing from the ostium secundum of the embryo and functioning in fetal life to allow the passage of considerable blood directly from venous to arterial circulation without going through the lungs. It closes soon after birth and usually becomes sealed within the first three months of life. In many cases it remains anatomically slightly patent as a valve slit, but as such it is functionally inactive. When the slit opening is small the patent foramen ovale is of absolutely no importance, but if it is moderately large and the right atrial pressure is much raised, venous blood may pass into the left atrium and even occasion slight cyanosis. Clinically unimportant patency of the foramen ovale has been reported in nearly one quarter of all autopsied cases (with a range from about one eighth to one third).

In a few cases the foramen ovale remains really patent and in such cases it may prove to be of some importance. In one series of 500 hearts (250 from white and 250 from Negro subjects), probe patency of the foramen ovale was found in 85 cases (17 per cent) while in only 2 cases (0.4 per cent) did the valvula foraminis ovalis actually fail completely to cover over the foramen ovale (Seib, 1934). Wide patency is usually associated with and probably caused by other more important congenital abnormalities, such as pulmonary stenosis or transposition of the great arterial trunks, or with acquired mitral stenosis, and these other defects determine the course and prognosis. Of a

[2] The terms "atrial septum" and "ventricular septum" are used interchangeably with "interatrial septum" and "interventricular septum," respectively.

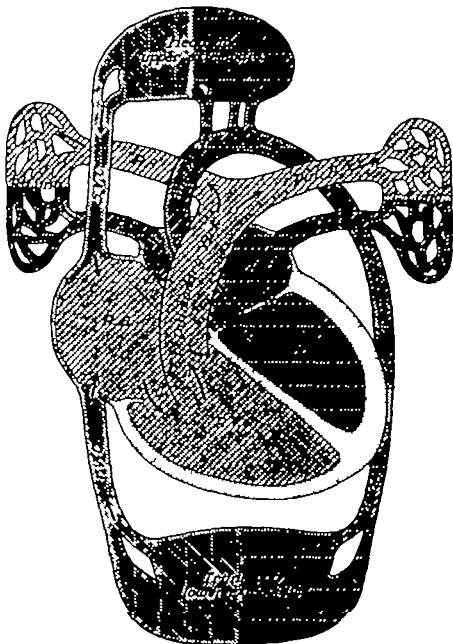


FIG. 66 Diagram of atrial septal defect. (Kindness of Dr Helen Taussig, Johns Hopkins Hospital, Baltimore, and The Commonwealth Fund, New York City)

series of 290 cases of patent foramen ovale (Abbott, 1931) only 40 were instances of pure or primary patency

Atrial septal defects of importance are those that involve relatively large areas of the septum (1) The *primitive ostium primum* in the lower part of the septum (36 cases in Abbott's series of 1 000 individuals with congenital cardiovascular defects, 18 of the 36 complicating other defects) or (2) the *primitive ostium secundum* (from which the foramen ovale develops) in the upper part of the septum (19 cases of Abbott's series, 9 of which complicated other defects) or (3) *absence of the entire atrial septum*, giving a three chambered or *triloculate heart* (*cor triloculare biventriculare*) if there are two ventricles, or a two-chambered or *biloculate heart* (*cor biloculare*) if there is but one ventricle (15 cases of the former and 14 of the latter in Abbott's series) Females showed a slight preponderance (44 to 35) in these three categories of atrial septal defect in Abbott's series. All these lesions are more serious than patency of the foramen ovale, persist from an earlier stage of fetal life, and are often complicated by other anomalies. Persistence of the ostium primum is not only more common than that of the ostium secundum but it is also much more serious (Figure 66 opposite page 310)

The explanation of the increase in size and work of the right heart chambers in these cases is that extra blood, often in large amount, enters the right atrium from the left atrium through the septal defect· this direction of flow has been assumed to be due to a slightly higher pressure in the left atrium but Uhley (1942) has shown that an important, perhaps the most important, cause of this direction of flow is the effect of gravity the right atrium being anatomically situated below the left, the septum lying more or less horizontally

In the cases of persistence of the primary and secondary ostia there may be no symptoms or signs and the subjects may live fairly long lives, though not so long as those with foramen ovale patency Enlargement and failure of the right ventricle are, however common. Loud systolic murmurs, rarely accompanied by thrills, are found in most of the cases, chiefly in the pulmonary valve area. Years ago they were ascribed to the septal defect itself but it has become evident that they are due to the dilatation of the pulmonary artery which is secondary to the increased pulmonary circulation or to a complicating mitral valve defect. With large atrial defects, the electrocardiogram shows marked right axis deviation (Figure 67) and the roentgen ray shows enlargement of the right atrium, right ventricle and pulmonary artery and its branches large and small, and also hypoplastic aorta (Figure 68) it is probable that in some cases at least twice as much blood passes through the pulmonary circulation as through the systemic. Paradoxical embolism may occur Cyanosis is infrequent but may appear as an occasional or terminal event when the right atrial pressure becomes greater than that in the left atrium, or constantly if there is a complicating pulmonary stenosis.

An analysis of 53 cases of atrial septal defects, 10 with necropsy control (Bedford, Papp and Parkinson, 1941) showed a preponderance of females in the ratio of 4 to 1 the age of death mostly from 30 to 50 years, and the

cause of death in the autopsied cases congestive heart failure in 3 pulmonary infarction in 2 embolism (one paradoxical) in 2, subacute bacterial endocarditis (a very rare complication) in only 1 bronchopneumonia in 1 and surgical operation in 1 the upper part of the septum was involved in 8 of these 10 cases. A pulmonary systolic murmur was found in 32 of the entire series and an accentuated pulmonary second sound in 31 followed by a diastolic murmur (probably due to a stretching of the valve ring) in 10. Slight or late cyanosis was present in 31 cases. Excessive pulsation of the lung hilum was noted by roentgen ray in 31 of the 50 cases so studied but a hilar dance was observed in only 5 Normal rhythm was the rule, being present in 47 cases

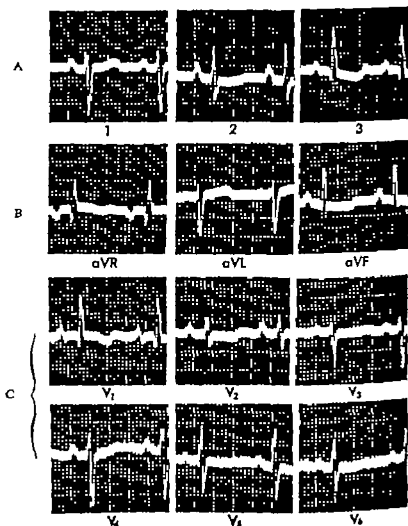


FIG. 67 Electrocardiogram in case of atrial septal defect, female, age 26. (A) Bipolar limb leads 1 2, and 3 (B) unipolar limb leads, VR, VL, and VF (C) six precordial leads, V to V inclusive. Time = 0.04 and 0.20 second amplitude 1 mm = 0.10 mv

Right ventricular preponderance was present in the electrocardiogram in 41 cases and complete right bundle branch block in 5 others.

When there is but one atrium, life is generally much limited, but some cases of remarkable longevity are on record with few symptoms or signs. Cyanosis is the rule, thrills and murmurs are infrequent, and dyspnea is inconstant. Of 5 cases with one atrium and two ventricles cited by Abbott one lived to the age of 31 years, the mean duration of life was 6 years. Of 9 cases with



FIG 68 Roentgenogram of thorax of case of congenital defect of the interatrial septum, showing extreme degree of dilatation of the pulmonary artery and its branches right and left, along with enlargement of the right ventricle. Note the shadows of cross sections of arteries. Small aorta. (Kindness of Dr Hugo Roesler Temple University Philadelphia.)

one atrium *and one ventricle the oldest case was 16 years at death and* the mean age was 3¼ years.

A very interesting association is that of *mitral stenosis with a defect of the interatrial septum* (Abbott, 1915 Lutembacher 1916) There is a combined effect of both lesions. The left atrium tends to remain small and the right atrium becomes very large receiving as it does the extra blood from the left atrium as well as from the great veins. There have been noted murmurs ove- the sternum or just to the left, presystolic and systolic in time, ascribed to th passage of blood through the septal defect, but it is naturally difficult t differentiate such murmurs from those due to the mitral valve disease an

transmitted thither; certainly the most common cause of the basal systolic murmur in such cases is dilatation of the pulmonary artery which is invariably present. The congenital deficiency of the atrial septum has been given credit for relieving somewhat the burden imposed on the pulmonary circulation and right ventricle by marked mitral stenosis, and thereby aiding the prolongation of life. Remarkable cases of this combination of mitral stenosis and atrial septal defect are on record, including that of a woman of 74 years of age who had passed successfully through eleven pregnancies and three abortions (Firket, 1880) a woman of 61 years who had gone through seven pregnancies without heart failure (Lutembacher 1916) and two other cases aged 74 and 62 years respectively (Bonnabel, 1906) However interatrial septal defects alone, if large, impose a serious burden on the right heart and pulmonary circulation, and therefore it does not appear likely that they can aid much in relieving the heart or lungs in the presence of mitral stenosis, except probably to prevent attacks of acute pulmonary edema which are an infrequent but distressing complication of tight mitral stenosis when the heart beats too rapidly

A large atrial septal defect is always to be suspected when there is the combination of a loud pulmonary systolic (not continuous) murmur marked prominence of the pulmonary artery and lung hilus shadows and small aortic shadow by roentgen ray and pronounced right ventricular preponderance by electrocardiogram in a person in fairly good health save for a variable amount of dyspnea. In differential diagnosis it may be said that the cor pulmonale due to pulmonary disease or endarteritis gives less right axis deviation and less lung hilus engorgement, while mitral stenosis is, of course, attended by its characteristic diastolic murmur

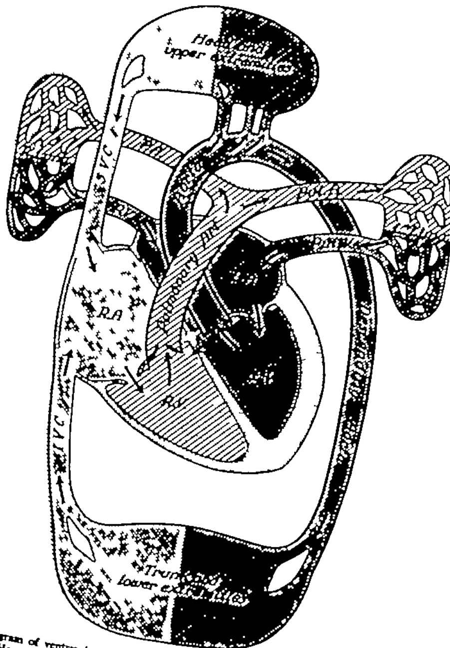
Surgical correction of uncomplicated but important atrial septal defects is now on trial and has been successful in a few cases (Murray 1948) [a] Correction of the atrial septal defect was done by passing sutures through the anterior wall beginning to the right of the aorta and pulmonary artery to emerge posteriorly through an area between the superior vena cava and right pulmonary veins. These sutures were tied together posteriorly drawn taut, and tied down firmly thus compressing the anterior and posterior walls of the atria. In one of the cases described the right atrium diminished to at least one half its size in two minutes the patient s condition was improved.

Ventricular Septal Defects

Next in frequency after atrial septal defects come ventricular septal defects, of which in Abbott s series there were 315 instances, including localized openings, isolated or complicated (274 cases) complete absence of the septum in the biloculate heart (14 cases) and in the triloculate heart with one ventricle and two atria (27 cases)

Localized ventricular septal defects are generally associated with other

[a] In March, 1951 Murray (personal communication) stated that he had performed the operation of closure of an atrial septal defect in seven cases with considerable improvement in three, some improvement in two, and death in t o.



o. 69 Diagram of ventricular septal defect. (Kindness of Dr Helen Taussig, Johns Hopkins Hospital, Baltimore, and The Commonwealth Fund, New York City.)

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congenital defects and are almost invariably found at the base of the heart just below the aortic valve in the region of the so-called undefended or fibrous space. Of the series of 274 cases collected by Abbott the ventricular septal defects were in this basal position in all but 17 and these 257 basal defects complicated other abnormalities in 207 cases, leaving 50 instances of the pure defect. Seven of the 207 complicated cases had but a right-sided (dextro-) position (Rechtslage) of the aorta as an additional defect, constituting the Eisenmenger complex while 51 had pulmonary stenosis with aortic dextroposition in 32, constituting the tetralogy of Fallot. These complications are important in that they favor cyanosis the dextroposition of the aorta is especially significant in this respect. The sexes are about equally represented in pure interventricular septal defects of Abbott's series of 50 cases 21 were male, 26 were female, and the sex of 3 was not stated.

The pure ventricular septal defect is usually small and more or less circular or oval, 1 to 2 cm in diameter (Figures 69 and 70) Its septal edge is often thickened and fibrous and the endocardium of the right ventricular wall opposite the opening is also similarly affected, probably by the repeated impact of the blood stream from the left ventricle. The right ventricle is usually somewhat enlarged (hypertrophied and dilated) and the pulmonary artery is slightly dilated, the left ventricle also may be bigger than normal. The shunt through the uncomplicated septal defect is arteriovenous, that is, left to right, except under unusual conditions.

There are no symptoms of pure ventricular septal defects unless they are very large, and in rare cases there are no signs. Usually however there is a loud blowing systolic murmur heard best just to the left of the midsternum and not widely transmitted. When the murmur is very loud there is a palpable thrill also, but this is occasionally absent. Cardiac enlargement may or may not be evident on physical examination and by roentgen ray The electrocardiogram is normal except in a few cases with abnormal right axis deviation and in rare cases in which the septal defect is associated with abnormality of the atrioventricular bundle (of His) with resulting congenital heart block. Cyanosis is rare in the case of uncomplicated ventricular septal defect and is practically only a terminal condition, the shunt being reversed to become venoarterial, or right to left, when the right ventricular pressure exceeds that in the left ventricle in pneumonia or some other such complication. Infrequently when the septal defect is large the whole heart may be much increased in size and fail with characteristic congestive signs and symptoms, including dyspnea.

An isolated interventricular septal defect has been called *Roger's disease* (Roger 1879) and the murmur caused by this defect has been called *Roger's murmur*

Roger H. "Recherches cliniques sur la communication congénitale des deux cœurs par inocclusion du septum interventriculaire." *Bull. de l'Acad. de méd.*, 1879 2me sér VIII, 1074

The following conclusions of this original publication are of interest (translation by myself)

I There is a *developmental defect of the heart* from which cyanosis does not result in spite of the communication between the two ventricular cavities and in spite of the free mixture of venous blood with arterial blood. This congenital abnormality which is compatible even with a long life, is a simple one, without the coexistence of congenital pulmonary stenosis. It consists of a defect (opening) in the interventricular septum.

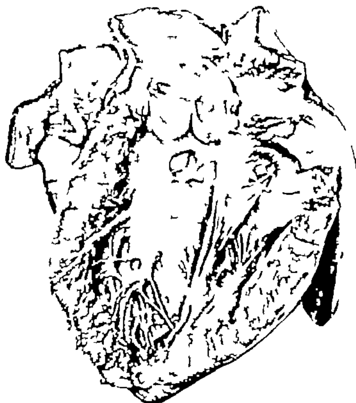


FIG. 70. Photograph of the heart of a boy showing a congenital interventricular septal defect of small size just below the aortic valve. The child had typical loud systolic murmur (Roger's murmur) with thrill at the left border of the sternum, maximal in the third and fourth intercostal spaces.

"2. It is important to distinguish this cardiac anomaly which I have recently been the first to study clinically not only from other malformations but especially from acquired heart disease. It is revealed only on auscultation, by a physical sign with very special characters this is a long loud murmur (produced by the passage of blood through the interventricular opening and directly into the pulmonary artery or the aorta, the site of which is frequently abnormal in these cases) This murmur is uncomplicated by other murmurs, it begins with systole and is prolonged to such an extent that it entirely covers the natural tic-tac of the normal heart sounds. It has its maximum intensity neither at the apex (as in the case of

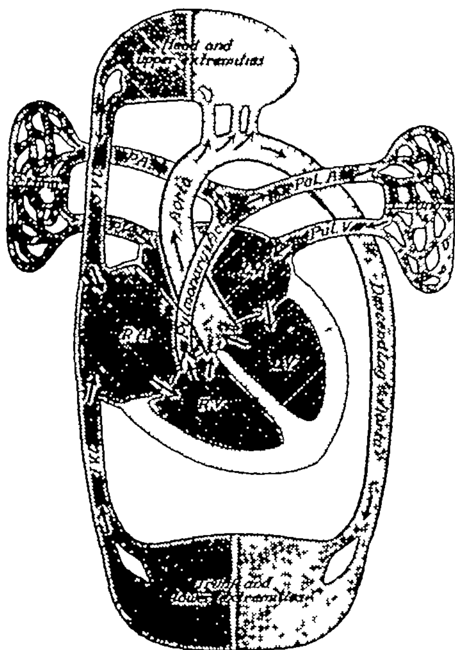


FIG. 71. Diagram of tetralogy of Fallot. (Kindness of Dr Helen Taussig, Johns Hopkins Hospital, Baltimore, and The Commonwealth Fund, New York City)

lesions of the auriculoventricular orifices) nor at the base to the right (as in aortic stenosis) nor to the left (as in pulmonary stenosis) but over the upper third of the precordial region. It is chiefly median in position like the septum itself and from this central point it diminishes in intensity uniformly as one moves the stethoscope over the chest. The murmur is not transmitted to the vessels. It coincides with no other sign of organic disease except the *harsh thrill* which accompanies it. This murmur is *the pathognomonic sign of an interventricular septal defect.*

"3 *The differential diagnosis* of this malformation (until now unrecognized or confused with other congenital or acquired lesions) will be henceforth rendered easy by attentive comparison of the physical signs. These signs vary in number site, and characteristics in heart disease when structural changes are multiple, progressive, and changing, while the murmur in question, like the permanent unchanging lesion causing it, remains without modification for an indefinite time. The same statement is true in comparing this murmur with signs of functional disorders such signs are very variable according to the diverse periods of cardiac weakness, and they are totally dissimilar in their acute or chronic nature from the constant signs of defective interventricular septum which change hardly at all with the years and increase only very slowly and almost insensibly

4 The consideration of the age of the subject is a capital point in the diagnosis; endocarditis, for example, shows itself almost never in infancy before the age of two years, and on the other hand the anemia of very young children is almost never attended by a heart murmur The result is that a *murmur in a nursing infant* is almost a certain indication of an *anomaly* of the heart or great vessels.

5 The *prognosis* is in general less grave in the malformation described above than in other organic diseases of the heart, in which the danger for children is greater and nearer permitting hopes for scarcely more than another decade of life. In spite of the presence of an uncomplicated interventricular septal defect, individuals can reach and even surpass the average duration of human life.

"6. An exact diagnosis ordinarily demands in heart disease an active, persistent *treatment* If on the other hand there is a congenital malformation of the heart, vigorous treatment is useless and even harmful. To show thanks to precision in diagnosis, when to act in one case and when to refrain in another is to render a service not only to physicians but also to patients.

It is of interest to note that Roger first described the condition and murmur that go by his name without having correlated in the same patients clinical and postmortem data. He had made observations, clinically and pathologically but not in the same cases. Later however his deductions were confirmed.

Although an interventricular septal defect is theoretically not a serious lesion, it is a handicap which shortens life. In Abbott's series of 50 "pure" cases, the mean duration of life was only 14½ years, the oldest case being 49 years old. One of the chief reasons for this shortening of life has certainly been in the past subacute bacterial endocarditis which Gelfman and Levine (1942) found to have complicated 57 per cent of 14 autopsied cases. With prophylactic use of penicillin and of other new specific therapy against infections this situation will be radically changed and the prognosis will doubtless be very much brighter especially since the septal defect itself causes

relatively little strain on the heart. Protection of such a patient is especially needed at the time of dental extraction when 300 000 units of penicillin should be injected intramuscularly 1 hour before the extraction and again 3 hours after to get rid of any alpha hemolytic streptococci that may get into the blood stream. If subacute bacterial endocarditis is already present, involving the edge of the defect in the right ventricle or the tricuspid valve or adjacent ventricular endocardium opposite the opening, penicillin in large dosage (800 000 to 1 000 000 units a day) should be given for several weeks or if ineffective, multiplied several times or supported or replaced by streptomycin. For details of this therapy consult Chapter 15 Subacute Bacterial Endocarditis.

Treatment of a pure isolated ventricular septal defect by surgery was hardly dreamed of when the first three editions of this book were published, but now it is only a matter of time before such correction becomes a practical routine already animal experimentation has demonstrated its possibility and the first successful attempts have been made in man (Murray 1948)[4] The technic as described by Murray consisted of introducing a strip of fascia lata into the right ventricle and attaching it to the septum. The details of this delicate operation are described by him in the Annals of Surgery 1948 XXVIII 843

Still more important will some day be the prevention of this as well as other congenital cardiovascular anomalies by the prevention or early cure of diseases, virus (like rubella) and otherwise, that beset the mother during the critical stage of the fetal heart development in the first trimester of pregnancy

The tetralogy of Fallot. This commonest of all combinations of congenital cardiac defects and one of the most serious has already been presented in part as an interesting and characteristic malformation in the early pages of this chapter (page 290 and Figure 64 page 299) but it belongs in the group of ventricular septal defect variations and so will be further discussed here (Figure 71) As noted above, the four essentials of this relatively common anomaly are (1) a high ventricular septal defect, (2) a dextroposed aorta overriding the septal defect, (3) stenosis of the pulmonary valve or of the right ventricular infundibulum below it, and (4) a much hypertrophied right ventricle It was encountered in 85 of Abbott's 1 000 autopsied cases of congenital defects of heart and great vessels. There are always cyanosis and finger clubbing from earliest childhood, often intense, the cyanosis being increased by exercise which readily distinguishes it from the slaty-blue color of argyria which is decreased when the skin flushes after exercise. Shortness of breath, a tendency frequently to squat, weakness, and faintness or even syncope are usual symptoms. A moderate to loud pulmonary systolic murmur on auscultation, blunt shoe-shaped heart with prominent aorta and decreased pulmonary vascular shadow on x ray examination (Figure 72) and marked

4 By March, 1951 Murray (personal communication) had operated to close ventricular septal defects in 13 cases with clear evidence of success in 7 (disappearance of murmur decrease of heart size, abolition of shunt as shown by cardiac catheterization, and increase of energy) 3 cases died.

right ventricular preponderance by electrocardiogram (Figure 73) complete the diagnostic evidence. Polycythemia and excessive hemoglobin, even up to double the normal, are in accord with the intensity of the cyanosis. Cardiac catheterization quickly reveals the dextroposed aorta into which the catheter

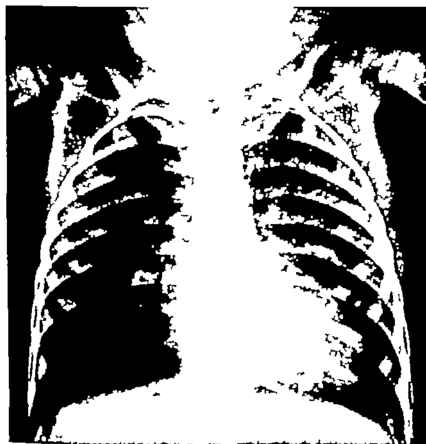


FIG. 72. Roentgen film of the thorax in case of tetralogy of Fallot.

readily passes. There may be the complication of patency of the ductus arteriosus with the tetralogy of Fallot and, if so there is much less cyanosis. There is, in such cases, a continuous murmur to the left of the sternum with the aorta in its ordinary position, but with a right-sided aorta the murmur is to the right of the upper sternum.

The prognosis of the tetralogy of Fallot is generally bad for a long life, the average duration in Abbott's series of 85 cases being 12 years, but a few patients reach middle age and one established the record of 59 years and 8 months (White and Sprague, 1929) Fatal complications include cerebral abscess, cerebral thrombosis, bacterial endocarditis, respiratory infections, and right heart failure.

The treatment was stated in the first three editions of this book to be only ordinary common sense protection of a cardiac cripple, but in the few years that have elapsed since then a great advance has been recorded. Blalock and Taussig in 1945 introduced a surgical operation that has greatly ameliorated the symptoms and signs of the disease although they have not cured it. The

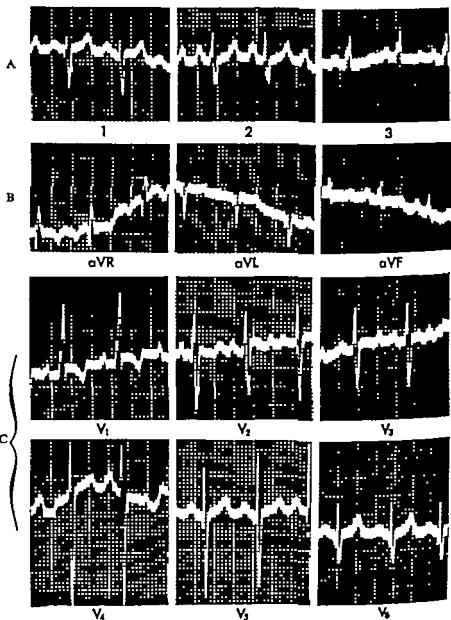


FIG. 73 Electrocardiogram in a case of tetralogy of Fallot, male, age 3 (*A*) Bipolar limb leads 1 2, and 3 (*B*) unipolar limb leads, aVR, aVL, and VF (*C*) six precordial leads, V to V inclusive. Time = 0.04 and 0.20 second amplitude 1 mm = 0.10 mv

procedure consists of the anastomosis of the right or left subclavian artery or in a few instances of the innominate artery to one of the pulmonary arteries, thereby bringing blue blood into the lungs for oxygenation, largely if not wholly relieving the cyanosis, dyspnea, weakness, polycythemia, and clubbing of the fingers in a most dramatic way At the time of writing 1 045 cases of the morbus caeruleus, mostly consisting of the tetralogy of Fallot or some variation thereof had been subjected to this operation in Blalock's clinic with a mortality of approximately 18 per cent and a high degree of improvement in the majority of the survivors (Blalock, personal communication, 1951)

Another technic to aid the victims of the tetralogy of Fallot in a similarly effective way has been introduced by Potts (1946) and consists of a somewhat simpler procedure of side to side anastomosis of aorta and pulmonary artery This operation of Potts has one particular advantage over that of Blalock in that it may be easily carried out in very young infants who might readily expire as a result of the tetralogy of Fallot before they reach the age in which Blacock's anastomotic operation is feasible In both types of operation, however, it should be noted that a new defect has been introduced by the surgical procedure amounting essentially to a left to right shunt which acts like an arteriovenous communication to increase the work of the heart. Taussig (1948) has demonstrated by x-ray the increase in heart size that follows the operation even while great improvement is shown by the child. Also a continuous murmur resembling that of a patent ductus arteriosus results from the operation. Despite this unfavorable point, the life of these children has undoubtedly been prolonged, though just how much it is still impossible to say The most suitable age for either of these two surgical procedures is probably between 6 and 18 although successful results have been noted earlier and later A more recent surgical procedure has been introduced by Brock (1948) and consists of valvulotomy of the stenosed pulmonary valve: the clearing of cyanosis has been noted in a few cases but it is still too early to evaluate this therapy

An important though not very common complication of the tetralogy of Fallot is subacute bacterial endocarditis, and therefore the same advice about the therapeutic and prophylactic use of penicillin given for a localized pure ventricular septal defect (see above) should apply here.

Finally as stated in the general discussion of congenital heart disease the most important consideration of all is that of the prevention of such a malformation as the tetralogy of Fallot. This will doubtless depend in large measure on the protection of the mother from various deleterious influences including virus infections (such as rubella) during the first three months of pregnancy

The Eisenmenger complex. Another but much rarer variation of the group of ventricular septal defects is that described by Eisenmenger (1897) consisting of this defect overridden by a dextroposed aorta and accompanied by a large right ventricle but with no pulmonary stenosis. There were only 7 such cases in Abbott s series of 1 000 in contrast to the 85 patients with the

tetralogy of Fallot. The symptoms and signs are much the same, however in the two conditions though generally less pronounced in the case of the Eisenmenger complex, which lacks the loud pulmonary systolic murmur and which also shows a normal or even somewhat prominent pulmonary vascular tree on x-ray examination.

The prognosis with this complex is still not good but in Abbott's series was far better than that of Fallot's tetralogy the mean age being 25 years as contrasted with 12 years. On the other hand, there is as yet no surgical correction here because a considerable amount of blood does go to the lungs; the difficulty consists in the equally large amount of blue blood that enters directly into the systemic circulation.

Entire absence of the ventricular septum so that the heart is three-chambered (**cor triloculare biatriatum**) or two-chambered (**cor biloculare**) is rare. Surprisingly efficient circulation is possible even with such marked deformity and cases surviving to adult life are on record. Although in these cases there is but one ventricle the course of the two blood streams entering it from the atria is often so directed in relation to their inflow and outflow tracts that they may actually mix but relatively little and so not conduce to much of any cyanosis or immediately serious disability of the circulation. In Abbott's series of 5 cases with one ventricle and two atria, one lived to be 31 years old and the mean age was 6 years. There are usually no murmurs or thrills in such cases, the cyanosis may be but slight or even absent, and the heart may be but little enlarged, rendering the diagnosis difficult or impossible. The cor biloculare occurred in 9 of the 1 000 cases of Abbott's series the mean age at death was 3¼ years and the oldest case lived to be only 16

To be distinguished from a congenital interventricular septal defect there occurs rarely a septal defect due to inflammatory ulceration through the upper septum in bacterial endocarditis or following coronary thrombosis. Such a lesion is relatively small and usually of little importance as a complication of fatal bacterial endocarditis, but it is a factor of added and serious and usually fatal strain in acute myocardial infarction.

An interesting and important rare complication of an interventricular septal defect is congenital heart block which has never been found without this structural lesion In itself it is not serious and is apparently compatible with a long life and full activity (Campbell, 1943) (see Chapter 34)

Anomalous papillary muscles and chordae tendineae. In rare hearts there exist unimportant anomalies of the papillary muscles and chordae tendineae, for example a papillary muscle found attached to the pulmonary valve in the routine autopsy of a man 69 years old (Collins, 1931) and a chorda tendinea extending across the left ventricular cavity from a small papillary muscle of its own to be attached well up on the aortic cusp of the mitral valve in a man of 40 years (Hamilton and Byers, 1899) The only importance of such cases lies in the occasional occurrence of unusual snapping intrasystolic sounds or twanging systolic murmurs, which may cause undue apprehension.

CONGENITAL MYOCARDIAL DISEASE

The heart muscle may be involved congenitally in a variety of ways. The most common change is that of hypertrophy with or without dilatation, secondary to various valvular septal, and vascular defects (for example, pulmonary stenosis, large interatrial septal defect, coarctation of aorta) This response to increased work and strain is comparable to that found in acquired valvular heart disease and chronic hyperpiesia. The muscle fibers are hypertrophied in whatever heart chambers are under particular strain, the right ventricle being by far the most commonly affected compared with the situation a decade or two ago. There are now but few cases of enlargement of this sort that are unexplained, these are grouped as congenital idiopathic hypertrophy There have been slowly separated from this group three other myocardial changes that are of importance. One consists of **necrosis and fibrosis** associated with hypertrophy explained on the basis of (1) infection and (2) anoxia, and most clearly evident in instances of very faulty anomalous blood supply as, for example, when the left coronary artery arises from the pulmonary artery A second myocardial change is that of the deposition of glycogen in large amounts in vacuoles in the heart muscle in the so-called **glycogen storage disease (von Gierke's disease,** von Gierke, 1929 Pompe, 1933) here the enlargement and glycogenization of the heart (Figure 74) are but part of the systemic disease of faulty glycogen metabolism with similar involvement of other organs in the body (especially the liver) fasting hypoglycemia, failure of hyperglycemic reaction, readily elicited ketosis and ketonuria, and early death. The third myocardial condition recently recognized is the dilatation, with secondary hypertrophy occurring in very young infants due to **excessively fast heart rates in paroxysmal tachycardia** (Hubbard, 1941) (see Chapter 32)

Congenital idiopathic hypertrophy of the heart. One of the least common congenital anomalies of the heart is that which has been called idiopathic hypertrophy The actual number of cases of "congenital idiopathic hypertrophy" has been steadily shrinking in recent years because of the special studies which have separated from it the rare cases of glycogen storage disease (von Gierke s disease—see above) myocarditis apparently of infectious origin (Kugel and Stoloff, 1933) instances of extensive myocardial necrosis with fibrosis such as that occasioned by a very abnormal coronary blood supply (Bland, White, and Garland, 1933) and cardiac enlargement secondary to formerly unrecognized paroxysmal tachycardia of excessively fast rates in infancy (see above and Chapter 32) There still remain a few unexplained cases.

The heart in congenital hypertrophy (idiopathic or not) is frequently two or three times the normal weight (75 gm, for example, instead of 25 gm at the age of 4 months) and may also be considerably dilated. In one of our own cases found to be due to glycogen storage disease the heart weight was five

times the normal, 175 gm instead of 34 (Figure 74) The cardiac enlargement is easily made out on physical examination and by roentgen ray The heart shadow is uniformly enlarged and roundish in shape, prominent to right of the midline as well as to left, and without particular dilatation of the atria or great vessels (arteries or veins) The electrocardiogram in uncomplicated cases is not remarkable, but with coronary anomalies it may be very abnormal (see end of this chapter)

The male sex is more frequently involved than the female. The course is

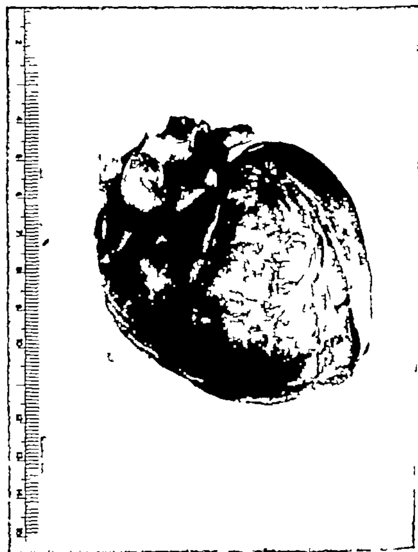


FIG. 74 Congenital hypertrophy of the heart due to glycogen storage (von Gierke's) disease. This heart of a 7-month-old infant weighed 175 gm instead of the average normal of 34 gm for this age. Both ventricles were enlarged but the shape of the heart was not significantly altered from the normal.

progressively a downhill one with symptoms and signs of circulatory embarrassment and weakness during the first year of life. Death comes rather suddenly or after increasing dyspnea or systemic venous congestion at about six months to a year or two of age the oldest patient of Abbott s series of 10 lived only four years.

There is no treatment as yet, but further study will doubtless reduce still more the number of cases of congenital idiopathic hypertrophy that are wholly unexplained.

CONGENITAL ENDOCARDITIS AND VALVULAR DEFECTS

Although acute endocarditis has been noted in the fetus and in the infant at birth, it is the late result of such inflammation that is much more frequently seen and which doubtless explains some congenital cardiac defects. Occasionally in cases with pulmonary stenosis, aortic stenosis, and other congenital valvular lesions, and rarely even in hearts without such lesions, the endocardium lining a part or the whole of a heart chamber may be thick and white due to marked fibrosis, the only adequate explanations of which are in most cases, a state of chronic anoxia or "strain" or a fetal endocarditis the deformed valves in such cases are also thickened and scarred as a rule.

Any heart valve or chamber may show this abnormality but the pulmonary valve and the infundibulum of the right ventricle are much more commonly involved than any other part of the heart, quite probably because of the fact that they bear the brunt of the chief cardiac circulatory effort in fetal life the aortic valve comes a very late second, while the mitral and tricuspid valves are affected only rarely In Abbott s series of 1 000 cases there were 150 cases of pulmonary or infundibular stenosis or atresia, 35 cases of aortic or subaortic stenosis or atresia, 19 cases of tricuspid stenosis or atresia, and but 11 cases of mitral stenosis or atresia. Only rarely except in the cases with aortic valve involvement, were the valvular defects uncomplicated, the reason for the relatively common uncomplicated occurrence of aortic or subaortic stenosis is probably its late development in the course of intrauterine life. Preponderant valvular regurgitation of congenital origin (involving the tricuspid, pulmonary or aortic valve) is excessively rare, as is also multiple valvular disease. Rheumatic valvular disease may infrequently be found as a complication of congenital heart disease.

Pulmonary valve or infundibular stenosis is in the vast majority of cases complicated by septal defects (101 of 110 cases in Abbott s series) most commonly ventricular alone (51 of Abbott s cases) less often both atrial and ventricular (34 of Abbott's cases) and rarely atrial alone (16 of Abbott's cases) Quite often it is associated not only with a ventricular septal defect but also with dextroposition of the aorta and marked right ventricular enlargement to form the tetralogy of Fallot (see page 318) The signs, course, and prognosis vary greatly according to the degree of the pulmonary valve or infundibular stenosis and of the associated anomalies, particularly the degree

of aortic dextroposition. When pulmonary stenosis is a part of the tetralogy of Fallot, cyanosis is invariably present with an atrial septal defect, cyanosis and finger clubbing are less than in the case of the tetralogy of Fallot, but when pulmonary stenosis is independent of septal defects, which is a much rarer situation, cyanosis is not present until the right heart fails, on which occasion stasis in the peripheral circulation is the explanation. The characteristic sign of pure pulmonary stenosis is a loud pulmonary systolic murmur with accompanying thrill. Congenital pulmonary stenosis has itself in recent years been relieved surgically in a considerable number of cases. Valvulotomy was introduced by Brock in 1948 Blalock has followed suit and reports (personal communication 1951) having operated upon 42 cases of valvular pulmonary stenosis with intact ventricular septum, with 8 deaths.

Congenital pulmonary regurgitation is very rare (see Chapter 26 for signs of this valve defect) it may complicate pulmonary or infundibular stenosis. **Pulmonary valve atresia** (closure) is always attended by other compensatory anomalies it allows but a very few years of life as a rule, the mean age in Abbott's 40 cases being 4 years and the oldest 30 years.

Aortic valve or subaortic stenosis is one of the rarer congenital anomalies. It doubtless is sometimes wrongly diagnosed as acquired aortic stenosis, the signs and course of both are outlined in Chapter 26 The valve is no more frequently involved (11 cases of Abbott's series) than the infundibulum of the left ventricle just below the valve (subaortic stenosis) (12 cases of Abbott's series) **Congenital aortic regurgitation** of any high degree has not yet been reported, so far as I am aware in slight degree it may complicate aortic stenosis or the dilatation of the aorta encountered in the tetralogy of Fallot. **Aortic valve atresia** is incompatible with life for more than a few months at best (maximal age of the 12 cases of Abbott's series 15 weeks, mean age 8 weeks) there must of necessity be a compensatory patency of the ductus arteriosus.

Mitral and tricuspid valve stenosis and atresia are rare anomalies almost always attended by compensatory septal defects. The average duration of life in cases with these anomalies is short. The commonest of these defects is tricuspid atresia, of which there were 16 examples in Abbott's series, the oldest survived to the age of 56 years. There were 3 cases of tricuspid stenosis *(the oldest 28 years of age) 6 cases of mitral stenosis (oldest 77 years)* and 5 of mitral atresia (oldest 3½ years) Clinical recognition of defective development of the right ventricle associated with tricuspid atresia or hypoplasia has been established (Taussig, 1936) the diagnostic criteria consist of cyanosis in infancy much diminished roentgen ray shadows of right ventricle and pulmonary artery left axis deviation by electrocardiogram (Figure 75) and absence of murmurs. It is to be treated surgically by Blalock's or by Potts operation as in the case of the tetralogy of Fallot (q v for details) In very young infants Potts operation is more suitable than Blalock's and may be lifesaving prior to the time of the arrival at the age when the more complicated procedure is feasible (Gasul, et al., 1949) **Tricuspid regurgitation**

has been described and is due to displacement of the attachment of the cusps of the valve (Ebstein, 1866 Yater and Shapiro, 1937)

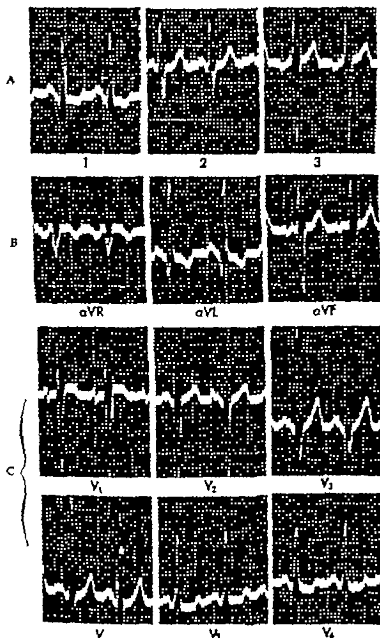


FIG. 75. Electrocardiogram in case of tricuspid stenosis, male, age 7 years. (*A*) Bipolar limb leads 1, 2, and 3 (*B*) unipolar limb leads, aVR, aVL, and VF (C) six precordial leads, V to V inclusive Time = 0.04 and 0.20 second amplitude 1 mm = 0.10 mv

CONGENITAL PERICARDIAL DEFECTS

There are several types of pericardial abnormality of congenital origin, all rare. These include absence or defects of the parietal pericardium (30 cases in Abbott's series) and diverticulum or hernia (6 cases in Abbott's series)

The parietal pericardium may be entirely absent so that the heart lies in the left pleural cavity along with the left lung, or it may be defective in part, most commonly over the region of the pulmonary artery In the case of ectopia cordis there may or may not be a pericardial sac: the cases with better prognosis have such a sac. When the parietal pericardium is absent the heart is usually freely movable, both on respiratory movements and with changes of body position physical examination and especially roentgen ray study may reveal this extreme mobility The clinical significance of absence or defect of the parietal pericardium is practically nil in itself, normal duration and activity of life being possible without any cardiac strain or circulatory embarrassment. Two complications may arise, however One is due to close contact of heart with left lung and pleura so that disease of the latter may seriously affect the former and vice versa, there no longer being protection by an intervening cavity Pleurisy with effusion, empyema, and pneumonia have been reported as fatal illnesses in the cases on record with absence or deficiency of pericardium. Another complication of importance that has been reported resulting in pain or even death, is sudden kinking of the great vessels, due to the fact that the heart is so freely movable.

The other two congenital anomalies of the pericardium, diverticulum and absence of attachment, are very rare and of no clinical importance when they do occur except that occlusion of the orifice, and consequently distension of the cavity of a pericardial diverticulum may interfere somewhat with the heart's action.

CONGENITAL ANOMALIES OF THE AORTA

Congenital aortic anomalies, found mostly in young persons, are due to maldevelopment in fetal life or at birth and include hypoplasia, coarctation, right aortic arch, double aortic arch, aneurysms, and transposition of the aorta and pulmonary artery as well as septal defects between aorta and pulmonary artery right ventricle, or auricle, and patency of the ductus arteriosus.

Aortic Hypoplasia

Hypoplasia (ὑπό, under and πλάσις formation) or small caliber of the aorta throughout its course is one of the commonest of the congenital aortic anomalies, but in high degree it is relatively rare and it is then usually associated with other congenital cardiovascular defects. In Abbott's series it was found in

77 cases, 75 of which showed other defects the commonest associated abnormality was an atrial septal defect. With such a defect there is a combination of a very large pulmonary artery and a small aorta due to the overloading of the pulmonary circulation and the underloading of the systemic. There is general hypoplasia of the arterial system when there is much aortic hypoplasia, with a tendency to pallor slow and incomplete growth, and retardation of sexual development. Small heart size and large heart size have both been reported in this condition, and heart failure in youth is said to have resulted from the strain, due perhaps in part to a high degree of aortic narrowness but more probably to complicating congenital defects in the heart itself.

Coarctation of the Aorta

Coarctation (*co-* together and *arctare* to press or make tight) of the aorta is a localized narrowing of the aorta of greater or lesser degree in the vicinity of the insertion of the ductus arteriosus which sometimes remains patent. Morgagni (1761) was the first to record its discovery at autopsy It is a fairly common abnormality having been noted in 142 of Abbott's series of 1,000 cases of congenital cardiovascular defects, in 79 of which it was the primary lesion and in the other 63 a complication of other anomalies, slight grades are likely to be missed even on postmortem examination and are of no clinical importance.

Etiology and pathology There have been described two chief types of aortic coarctation, called the infantile and the adult, but there is not always a sharp separation between them. The first (or infantile) a rare type (37 cases in Abbott's series, only 9 of which were "primary") consists of narrowing of the whole isthmus, that is, that part of the aorta between the left subclavian artery and the ductus arteriosus, sometimes the proximal arch itself is also involved. In fetal life the isthmus has little function since blood enters the descending aorta largely through the ductus arteriosus therefore, it quite naturally remains hypoplastic. This fetal condition may persist for a few weeks or months after birth to a greater or lesser degree, but rarely is it found in adult life. In extreme cases it may be represented simply by a fibrous cord, the circulation to the lower part of the body being taken care of wholly in such cases by the patent ductus arteriosus which thus supplies only venous blood to the abdominal viscera and legs with resulting disability The infantile type is serious, usually associated with other important anomalies, and had been thought to be incompatible with long life, there having been a maximum of 9 months and a mean of 8 hours in Abbott's series of 9 "primary" cases. However recently Johnson and Kirby (1948) have reported using in three patients aged 13 17 and 20 years respectively the left subclavian artery to bridge the long gap of the coarcted aorta of the "infantile type" with success in one case, partial benefit in a second, and failure in a third.

The second (or adult) type of aortic coarctation consists of localized constriction of the aorta at, or most often just below the insertion of the ductus

arteriosus and rarely above that point (Figure 76) It is much more common than the infantile type, and less serious In Abbott's series there were 105 cases In only 35 of which the condition complicated other defects. It is probably always a prenatal condition, developing in the fetus. In only a few of the cases does the ductus arteriosus remain patent. There may be other congenital cardiovascular anomalies, especially when the coarctation is extreme

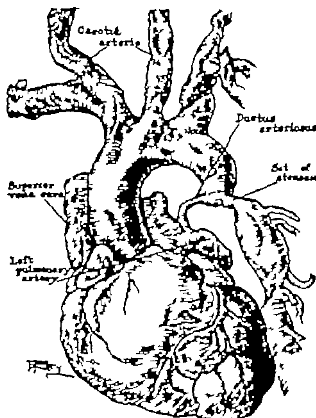


FIG. 76. Coarctation of the aorta (adult type) just below the ligamentum arteriosum. (Case of Dr W D Shelden.) (Blackford, "Coarctation of the Aorta, *Arch. Int. Med.*, May 1928)

but frequently the condition is uncomplicated The most common associated anomaly is the bicuspid aortic valve either congenital or acquired in origin, found by Abbott in 50 out of 183 collected cases (Abbott, 1928) and in 42 per cent of 104 additional autopsied cases reported by Reifenstein et al. in 1947 All grades of narrowing of the aorta occur from that which is so slight that it can scarcely be seen on careful postmortem scrutiny up to complete local aortic obliteration. Coarctation has been noted more often in the male than in the female, the adult type being three to five times more frequent in the male sex why this is so is not known. In a recent series of 96 cases reported at the Mayo Clinic (Christensen and Hines, 1948) there were 76

males and 20 females, this ratio is characteristic of other series. It has also been found in more than one member of a certain family (Walker 1934)

The result of pronounced coarctation of the aorta of the adult type on the circulation is of much interest. The aorta is usually considerably dilated above the constriction (sometimes with an aneurysm) and often but not always narrowed below A collateral circulation is developed, at times in high degree blood being carried to the lower part of the body by widely dilated, tortuous internal mammary scapular and intercostal arteries. The heart becomes enlarged in most cases and sometimes is markedly hypertrophied and dilated. Hypertension accompanying the coarctation is responsible for this cardiac hypertrophy as a rule, but on occasion acquired valvular disease, which is a not infrequent complication, may be an additional factor The arterioles in the muscle and skin of the arms in young subjects are normal and indistinguishable from those in the legs (Graybiel, Allen, and White, 1935) The hypertension usually found in persons with aortic coarctation need not be wholly ascribed to the defect directly but may be due in part at least to a secondary effect, namely the diminution of the renal blood flow below the constriction, which in turn causes a generalized vasoconstriction reflexly or through the production of the chemical mediator called hypertensin or angiotonin (see Chapter 19) (Steele and Cohn, 1938) when the collateral circulation is very richly developed the blood pressure may be perfectly normal, the renal circulation also then being adequate. The early hypertension in cases of aortic coarctation is sometimes attended by congenital intracranial aneurysms (as in the circle of Willis) Also unusual blood supply to the teeth has been reported in coarctation of the aorta.

Symptoms and signs. There are no particular symptoms of the adult type of coarctation of the aorta and often no signs, or so slight that the anomaly escapes notice during life. With high grades of coarctation, however there are a number of important signs (1) inequality of blood pressure and of pulse fullness and form between the upper and lower extremities, the brachial systolic pressure often being much elevated (even to 200 mm of mercury or more) while the femoral blood pressure is low (100 mm or less as a rule) and the femoral pulse is small, although the diastolic pressure levels may be much the same; (2) evidence of compensatory collateral circulation between the upper and lower parts of the body the internal mammary intercostal, scapular and deep epigastric arteries being much dilated, tortuous, and, in the case of the first three groups of vessels, easily felt and sometimes visibly pulsating (3) long systolic murmurs transmitted from the aortic coarctation itself heard not only over the precordium and back, but especially down the spine, where it may be heard to extend into diastole and also along the course of the dilated tortuous anastomotic vessels, sometimes accompanied by palpable thrills (4) decrease or absence of the shadow of the aortic knob by roentgen ray frequently with dilatation of the ascending aorta and first part of the arch (5) roentgen ray evidence of well-marked notching of the ribs due to the dilated tortuous intercostal arteries (Figure 77) and (6) enlargement of

the heart and sometimes signs of failure, due in part to frequent complicating heart lesions (especially acquired valvular disease) but in large part to the hypertension associated with the stenosis of the aorta. It should be reiterated that the brachial systolic pressure is not always high in cases of coarctation of the aorta but there is almost always a greater blood pressure in arms than in legs. Retrograde arterial or direct aortic Diodrast injections can helpfully outline the roentgen ray shadow of the coarcted aorta and of some of the collateral circulation for confirmation of the diagnosis and especially as guidance for the surgeon.

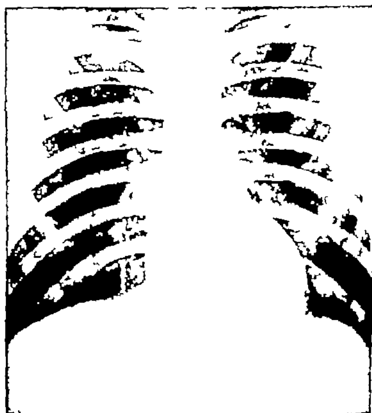


FIG. 77 X-ray photograph of a 19-year-old boy with coarctation of the aorta, demonstrating notching of the ribs and absence of aortic knob (Blood pressure in the arms 175/110 blood pressure in the legs 135/100.)

Course and prognosis. Complications. The course and prognosis of coarctation of the aorta vary enormously depending chiefly on the degree of narrowing of the aorta and the extent of the collateral circulation, but even when slight the condition is important because of the possibility of local infection in the form of subacute bacterial aortitis or endocarditis of a bicuspid aortic valve. *Marked coarctation is often a serious anomaly which may kill in youth by one of four complications heart failure, rupture of the aorta itself apo-*

plexy due to cerebral hemorrhage or thrombosis, and bacterial infection invading the area of coarctation or the aortic valve On the other hand, it is compatible with long life as in the case of a 92 year-old man with completely closed aorta (Abbott, 1928)

Of a series of 200 cases of the adult type collected by Abbott (1928) the average age at death was close to 32 years, with extremes of 3 and 92 years 60 died of congestive heart failure, 40 of sudden heart (2) or aortic (38) rupture, 26 of cerebral complications, and 14 of bacterial endarteritis. Of a more recent series of 104 autopsied cases (Reifenstein et al., 1947) 23 per cent died of rupture of the aorta, 22 per cent of bacterial invasion, 18 per cent of congestive heart failure, 11 per cent of intracranial lesions, and 26 per cent of incidental causes.

Between 5 and 10 per cent of cases with coarctation of the aorta have an associated patency of the ductus arteriosus, for example, 8 of 140 cases surgically treated by Gross (personal communication, 1950) 10 per cent of a series at the Mayo Clinic (Taylor et al., 1950) and 10 per cent of Abbott's cases.

Treatment. In the last edition of this book it was stated that there was no special therapy for congenital coarctation of the aorta, but that the subject should be protected as much as possible from physical strain and infections. In the intervening years there has occurred a great advance due to the introduction independently by Crafoord (1945) and Gross (1945) of surgical correction of the defect by excision of the area of coarctation and end to end anastomosis of the cut ends of the aorta in children and young adults where the narrowed portion is long the left subclavian artery or a vascular graft can be used to bridge the gap Postoperatively the blood pressures in arms and legs equalize at normal levels. Of the first 100 cases operated upon by Gross (1950) 11 died, and they were for the most part early cases, of the others 71 were completely relieved, 8 others satisfactorily improved, one unchanged, and 9 explored only (because of findings contraindicating operations on the aorta itself) Blalock has written to me (February 1951) of having operated upon 103 cases of coarctation of the aorta with 11 deaths.

Differential diagnosis. There is one condition with which coarctation of the aorta is commonly confused and that is hyperpiesia (essential hypertension) The differentiation is, however easy if one has in mind the possibility of the congenital defect, especially in a child or young adult the difference between the blood pressures of arms and legs, the systolic or continuous murmur transmitted down the upper spine the palpable intercostal artery pulsations, and the notching of the ribs seen by roentgen ray at once lead to the correct diagnosis.

Other Rare Congenital Aortic Anomalies

These are (1) localized weakness of the wall resulting in aneurysms, usually small, (2) transposition of the aorta and pulmonary artery so that the former

arises from the right ventricle and the latter from the left as the result of reversed torsion of the common arterial trunk in the course of fetal development, (3) a right-sided instead of a normal left-sided aortic arch and (4) a double aortic arch due to persistence of the right-hand side of the fourth primitive arch.

Congenital defects in the aortic wall. Congenital defects in the aortic wall with thinning and even outpocketing (aneurysm) are very rare and small. They are an incidental finding at postmortem examination and are of no clinical importance. The medial necrosis responsible for dissecting aneurysms does not belong here.

Transposition of the great arteries. Transposition of the great arteries is an infrequent anomaly found much more often in the male sex than in the female in the ratio of about 4 to 1 It is incompatible with survival for more than a few hours or days after birth unless there is a septal defect which allows some venous blood to reach the lungs such defect usually consists of a patent foramen ovale In some cases there is also an interventricular septal defect or a patent ductus arteriosus. When the ventricular septum is defective life may last for years, but the handicap is a serious one and death occurs almost always *before adult age is reached and is due to heart failure or complicating* infections. In Abbott's series of 1 000 cases of congenital cardiovascular defects there were 74 cases of complete transposition of the aorta and pulmonary artery in 49 of which it was the primary defect. Of these 49 cases, 32 had a closed ventricular septum with longest survival to 11 years, while 17 had a ventricular septal defect with longest survival to 16 years.

Cyanosis is an almost invariable sign of complete transposition of aorta and pulmonary artery except in early infancy when the cyanosis tends to be absent or less marked than later as is the case also in some other congenital cardiac anomalies the cyanosis sometimes becomes very marked and it is then accompanied by definite clubbing of the fingers. The heart is enlarged, particularly the right ventricle, and the electrocardiogram shows abnormal right axis deviation. Roentgenologic study may show little except the cardiac enlargement, but there may be some suggestion of the anomaly of the great arteries, especially in the oblique views. There may or may not be heart murmurs and thrills, dependent on the presence of other anomalies such as patency of the ductus arteriosus· uncomplicated transposition of the great arteries should not cause murmurs.

The antemortem diagnosis of complete transposition of the aorta and pulmonary artery is extremely difficult, but Taussig (1938) has pointed out the combination of four characteristic features (1) persistent cyanosis, (2) cardiac enlargement, especially of the right ventricle, (3) a narrow aortic shadow in the anteroposterior roentgenogram, and (4) an increase in the width of the roentgenographic shadow cast by the great vessels when the patient is placed in the left anterior oblique position.

A hopeful development in these very serious cases has taken place since the last edition of this book was published through the introduction by

Blalock of the production of an atrial septal defect and sometimes in addition the anastomotic operation which he has used in cases of the tetralogy of Fallot, namely joining subclavian and pulmonary arteries on the right. He has operated upon 62 cases, with 38 deaths the best results have been in patients with pulmonic stenosis as well as transposition and in patients with the Taussig Bing syndrome (Blalock, personal communication, 1951)

Corrected transposition of the great vessels. There is a condition called corrected transposition of the great vessels in which the aorta and pulmonary artery although in abnormal position regarding each other arise nevertheless from the correct ventricles. Such an anomaly in slight degree is of little or no clinical importance since the circulation is maintained practically in a normal manner and the condition may not be very obvious even at postmortem examination. When of marked degree, however it is associated with other anomalies such as interventricular septal defects, and life does not last beyond early adult years there were but 6 cases in Abbott s series, 4 of which were primary in type with longest survival to 24 years.

Finally a third type of transposition occurs, called **partial transposition**, in which both aorta and pulmonary artery arise from the same ventricle. As in the case of complete transposition with septal defect, there is frequently cyanosis Life is usually short in this condition, averaging 4/ years in 16 primary" cases collected by Abbott.

Right or double arch. Vascular ring. Anomalies of the aortic arch consisting of a right or double arch are rare and for the most part unimportant, except that there tends to be more or less compression of esophagus and trachea between the aorta and ductus arteriosus in the case of the right aortic arch, and between the two sides of the arch when it is double In some cases this obstruction is an important complication, and rarely it may be serious with *dysphagia* (called *lusoria* from the Latin, meaning deceitful) esophageal dilatation and ulceration, tracheal stenosis, and asphyxia. With obstruction of high degree and the diagnosis of right or double aortic arch established, surgical cure by transecting the constricting vascular ring has been effected by Gross (1945) since the last edition of this book was published. Dysphagia lusoria has also been noted in cases with certain other anomalies of the great arteries, for example, when the right subclavian comes off the descending thoracic aorta instead of the innominate artery The diagnosis must rest, in the main at least, on roentgen ray evidence of reversed position of the aortic arch or of its double character and on abnormal deviation or obstruction of the trachea and also of the esophagus as studied fluoroscopically during the ingestion of barium (Figure 78)

In Abbott s series there were but 5 cases of double aortic arch, the oldest surviving to 87 years, and 35 cases of right aortic arch, 14 classified as primary" with the oldest case 61 years females outnumbered males (8 to 5) in a small series of 13 cases of these two anomalies. Abbott recorded 7 cases in her total collection of 1 000 who showed the right subclavian artery arising from the descending aorta, and 8 cases with left subclavian artery arising

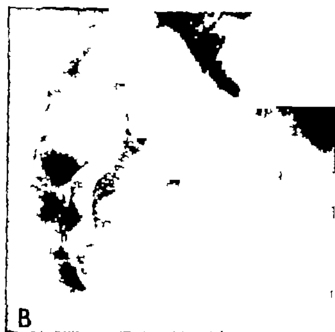


FIG. 78. Roentgenograms showing a right aortic arch displacing trachea and barium-filled esophagus forward and to the left. (*A*) Anteroposterior view. (*B*) right anterior oblique view. (Kindness of Dr. Hugo Roesler, Temple University, Philadelphia.)

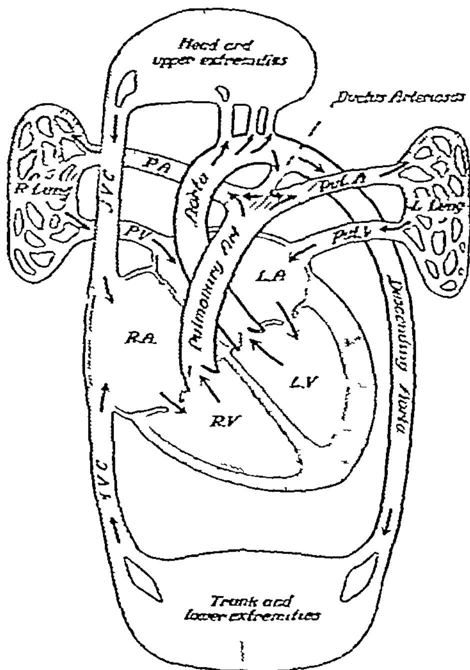


FIG. 79. Diagram of patent ductus arteriosus. (Kindness of Dr. Helen Taussig, Johns Hopkins Hospital, Baltimore, and The Commonwealth Fund, New York City.)

from either the ductus arteriosus or the pulmonary artery: in the former group one of 5 cases lived to be 44 the oldest age noted, while the one case of the latter whose age at death was noted was only 5 years old.

COMMUNICATIONS BETWEEN THE AORTA AND PULMONARY ARTERY

There are four types of congenital communication between the aorta on the one hand and pulmonary artery right ventricle, or right atrium on the other hand. They are first, and most common, patency of the ductus arteriosus second, rare cases of a persistent truncus arteriosus without separation into aorta and pulmonary artery: third, very rare instances of communication between the aorta and pulmonary artery by arterial septal defect and, fourth, very rare cases of communication between aorta and right ventricle or right atrium by septal defects. The possible rupture of the aorta into right ventricle or right atrium in bacterial endocarditis and endarteritis, or into the pulmonary artery in syphilitic aortitis, is discussed elsewhere (see Chapters 15 and 28 respectively)

Patency of the Ductus Arteriosus

The ductus arteriosus (also called *ductus Botalli* Botallo 1530) which normally in the fetus diverts most of the blood from the pulmonary artery into the aorta, should cease to function soon after birth, it should be converted within a few weeks into a fibrous cord, the *ligamentum arteriosum*. Its obliteration may however be delayed for some months, or it may persist as a patent arterial canal throughout life. Its patency may be regarded as a congenital anomaly if it is found later than three months after birth (Figure 79) It is one of the commonest of all congenital cardiovascular defects, ranking third in incidence (242 cases, 92 as the primary and 150 as a complicating defect) after interatrial and interventricular septal defects respectively in Abbott's series of 1 000 cases. Because of its curability now in childhood physicians in general have become much more familiar with its diagnosis. For the anatomic position of the ductus arteriosus see Figure 76, page 330.

Etiology *Cause* The cause of persistent patency of the ductus arteriosus is not always clear Frequently it appears to be a compensatory condition in the presence of some serious cardiovascular defect like infantile coarctation of the aorta or transposition of the great arterial trunks in other cases it is due to an unexplained arrest of development.

Age Beginning at birth it may last through a long life. It has been noted most often in children and young adults, the mean age at death of 92 cases of simple patency in Abbott's series being 24 years. It is frequently found in old people, the oldest autopsied cases on record being 66 years (Josefson, 1897 White, 1928) a man with this condition still in good health at 75 years has been followed by the author for 27 years, while another case reported by Walker and Ellis in 1941 then in good health at the age of 73 died suddenly

at the age of 78 five years later while mowing his lawn (there was no autopsy —personal communication)

Sex Patency of the ductus arteriosus has been found more often in the female sex, in the ratio of 2 to 1 (55 to 29 in Abbott s series of 92 cases of simple patency in which the sex was stated and 333 to 145 in Gross' series of 478 cases—Gross, personal communication 1951)

Pathology The patency of the ductus arteriosus varies very much in degree, from that of a fine canal barely admitting a small probe or bristle to that of large caliber easily admitting pencil or finger It may be very short, so that there is hardly more than a direct opening between contiguous aorta and pulmonary artery or it may be several centimeters long· usually it is ½ to 2 cm long. It may be cylindrical in shape, funnel-shaped, or conical, with wider end at the aorta, or it may be dilated to form a kind of aneurysm. In patency of the ductus arteriosus of long duration or of marked degree, especially in the combination of these conditions, the pulmonary artery is dilated and both ventricles are enlarged, with hypertrophy and dilatation, the blood flow from aorta to pulmonary artery increasing the work of both ventricles· in such cases the right ventricle has to overcome the pressure directed against its own blood stream and the increased blood flow through the lungs, and the left ventricle has to increase its output to make up for the diversion of a considerable amount of blood from the systemic circulation. It has been estimated that as much as 25 to 75 per cent of the blood pumped out by the left ventricle may be diverted into the pulmonary circulation via a patent ductus arteriosus. Atheroma with calcification is commonly found in the patent ductus arteriosus, especially at its mouth in the aorta and often also about its orifice in the pulmonary artery Very rarely spontaneous thrombosis may obliterate the ductus

The ratio of complicated to uncomplicated patency of the ductus arteriosus is about 2 to 1 In Abbott's series of 150 complicated cases it was found associated with coarctation of the aorta 13 times (6 out of 70 cases of the adult type, 7 out of 9 of the infantile type) with complete transposition of the great arterial trunks in 33 cases, with pulmonary atresia 28 times, with pulmonary stenosis 12 times, and with tricuspid atresia 6 times.

The ductus arteriosus may take an anomalous course or even be entirely absent. Rarely it gives off the left subclavian artery

Symptoms. There are no symptoms of patency of the ductus arteriosus itself, except in a rare patient who is conscious of the harsh murmur and thrill caused by the rush of blood through the ductus, and in occasional cases where the ductus is so large that there is retardation of growth or when dyspnea develops because the heart fails as it would from aortic regurgitation or a large arteriovenous communication.

Signs. Usually pathognomonic evidence of the condition is present. There are two important signs, one diagnostic, the other suggestive when both are present the diagnosis of patent ductus arteriosus may be regarded as certain.

The first sign is a continuous murmur usually loud with systolic accentuation, maximal over and often limited to the region of the pulmonary artery

at the second rib and intercostal space just to the left of the sternum and not so loud in the neck, and generally attended by a palpable thrill (in the absence of evidence of rupture of aorta into pulmonary artery) This murmur has been variously described as resembling the sound of a humming top of a mill wheel or other machinery of a train in a tunnel, or of rolling thunder It is almost invariably harsh, rarely blowing. In cases with a right aortic arch the continuous murmur is heard over the patent ductus at the right of the upper sternum instead of at the left. In some cases with wide ductus patency and a dilated left ventricle there may also be heard a mitral middiastolic murmur simulating mitral stenosis.

The second important sign is roentgenologic, consisting of unusual prominence of the heart shadow in the region of and just above the pulmonary artery (Figure 80) without increase in the size of the left atrium pointing to mitral stenosis, and without cyanosis which might result from pulmonary endarteritis obliterans. This abnormal bulging of the left upper border of the heart shadow is more pronounced in some cases of patency of the ductus



FIG. 80. Roentgenogram of thorax in case of congenital patency of the ductus arteriosus. Note the bulge in the region of the pulmonary artery J W male, now 75 years, with characteristic machinery murmur This film was taken 13 years ago, but there has been no change since

arteriosus than in any other condition except that of interatrial septal defect which presents much larger shadows of both pulmonary artery and lung hilus shadows without a continuous murmur. If there is but a narrow lumen through the patent ductus the roentgen ray sign may be minimal or absent while the typical murmur may be marked. If on the other hand, there is a very wide lumen with much blood flow the roentgen ray sign is marked and the murmur minimal or absent. In infants and rarely in young children the murmur may be absent or but slight and only systolic in time during the first few years of life; in adults it is almost invariably present as a typical continuous murmur but there are rare exceptions with systolic murmur alone.

Other signs are those associated with cardiac enlargement, which is found in some of the cases, various complications, and in a few cases a full pulse pressure due to low diastolic pressure when the patency is so wide that there is considerable aortic regurgitation into the pulmonary artery in diastole; a *wide pulse pressure in patency of the ductus arteriosus is, however, not the* rule and a water-hammer pulse is very rare.

Course, complications, and prognosis. Patency of the ductus arteriosus may be a condition compensating for the presence of some serious congenital defect like transposition of the great arterial trunks, thereby helping, together with septal defects, to prolong life. In such cases, however, life is short at best, lasting only a few years. Uncomplicated patency may or may not be an important burden for the heart. If it is of large caliber it is a serious condition leading to considerable cardiac enlargement and failure in youth. If it is of small caliber it may limit neither activity nor duration of life, death in old age being caused by some noncardiac disease. The oldest cases proved at autopsy were 66 years of age at death but two other cases have been known to have reached the middle or upper seventies (see above under etiology, age). *Always, however, patency of the ductus arteriosus is something of a menace* because of the likelihood of invasion by subacute bacterial (Streptococcus viridans) endarteritis which used to end fatally in the course of months, just as did subacute bacterial endocarditis, with which it may be associated. In Abbott's series of 92 "primary" cases of ductus arteriosus patency death was ascribed to subacute bacterial endarteritis in nearly one quarter, while Gelfman and Levine (1942) found 4 such cases (29 per cent) among 14 patients with patency of the ductus.

Rupture of a dilated pulmonary artery due to ductus arteriosus patency has been observed as a rare complication. Also paradoxical embolism has been noted, thrombi from the left atrium or vegetations from the mitral or aortic valves entering the pulmonary circulation by way of the patent ductus arteriosus. A reversal of current may sometimes occur, generally as a terminal event, when the blood pressure in the pulmonary circulation for any reason exceeds that in the systemic circuit. In infants there may be transient attacks of dyspnea and cyanosis when the pulmonary pressure is raised by crying and by holding the breath during nursing. Of 92 cases of Abbott's series, death in 40 was sudden or due to myocardial failure, in 21 to bacterial endarteritis or

endocarditis, in 3 to a cerebral lesion, in 3 to bronchopneumonia, and in the remainder unstated.

Treatment. A decade ago there was finally introduced what had been prophesied, namely specific treatment for patency of the ductus arteriosus. Surgical interference to ligate the ductus was successfully accomplished, and a new and dramatic era in the treatment of congenital heart disease began (Gross and Hubbard, 1939) The operation has now been carried out in many hundreds of cases by various surgeons throughout this country and abroad with very low mortality and with excellent results. Transection rather than simple ligation is now recommended by Gross (1947) although excellent results have been obtained by ligation. Surgical correction is now definitely indicated in all children and young adults to relieve the heart of strain and to avert the dangerous and common complication of subacute bacterial (Streptoccus viridans) endarteritis, but it must be recognized that there are some patients in whom the condition is inoperable (Shapiro and Keys, 1943) and that there still exists in any case a definite operative risk. Surgery has also been proved (Touroff and Vesell, 1940 and 1942 Bourne, 1941) to have a place, with or without chemotherapy in the cure of subacute bacterial infection of the ductus and pulmonary artery It is striking to note the disappearance of murmur and thrill after ligation of the ductus and in those cases with cardiac enlargement and increased pulse pressure even of such signs too and, on occasion, even of a mitral middiastolic murmur due to left ventricular dilatation. In those cases not operated upon, protection against infection and exhaustion is advisable. The routine use of penicillin to ward off bacterial endarteritis during infections and surgical procedures, including tooth extraction, is to be recommended as in the case of a ventricular septal defect (q v)

Differential diagnosis. In infants the condition may be undiagnosable In adults the distinctive murmur is almost invariably present, this murmur must be differentiated from the venous hum sometimes heard in the neck, especially on the right side in children, which hum may be transmitted downward over the upper chest but is quickly obliterated by compression of the neck veins, and it must also be distinguished from the murmur of an arteriovenous aneurysm, uncommon in the upper chest and usually located on the right side A rare condition accompanied by the continuous murmur characteristic of patency of the ductus arteriosus both in position and in character is rupture of an aortic aneurysm into the pulmonary artery the differentiation can be made by analysis of the clinical course. The roentgen ray sign of marked prominence of the pulmonary artery though helpful, is not pathognomonic of patency of the ductus arteriosus, for mitral stenosis, pulmonary fibrosis or endarteritis obliterans, and interatrial septal defects must be excluded before a sure diagnosis is justifiable.

Other Communications Between Aorta and Pulmonary Artery

The other communications between aorta and pulmonary artery are much less common. The first is the serious condition of a common arterial trunk (truncus arteriosus communis) with its accompanying intense cyanosis, absence of lung hilar shadows, and short life (averaging but 4 years in 21 cases analyzed by Abbott) A second is an opening between these two vessels above the valves, usually small and not so important (in Abbott's series 10 cases with survival to 48 years in the oldest) The third is a defect between the right sinus of Valsalva and the right ventricle, with or without an associated slight interventricular septal defect just below the valve, or between the posterior sinus and the right atrium. The defect may exist from birth or there may be in early life simply a thinned wall or aneurysm which may rupture fatally into the right ventricle (Hirschboeck, 1942) There are no symptoms caused by these anomalies. The signs in cases of the second and third categories above in which there are definite, though small, openings are much like those of patency of the ductus arteriosus with loud continuous murmur lower in position and very near the ear The cardiac strain results in enlargement, but the particular danger appears to lie in a serious complication of bacterial infection of the walls of the defect.

CONGENITAL ANOMALIES OF THE VEINS

Congenital anomalies of the veins are of little or no clinical importance. They are frequent in the case of the small veins and rare in the case of the venae cavae and chief pulmonary veins. The commonest defect of the great systemic veins is persistence of the left superior vena cava emptying into the right atrium by way of the coronary sinus (36 cases in Abbott's series, 27 of which complicated other defects) associated with it in most cases is the usual (right) superior vena cava, but sometimes it is alone and receives blood from the right side by way of an extensively developed vena azygos major In rare cases the single superior vena cava or the inferior vena cava is displaced to the left and opens into both atria at the point of a septal defect. Rarely also the left hepatic vein persists and empties into the anomalous left superior vena cava, which thus represents the persistent left sinus venosus of the embryo. Many different variations are possible in the case of the pulmonary veins (58 cases total in Abbott's series, all but 4 complicating other defects) The two right or two left veins sometimes coalesce before entering the left atrium, or one or more of the pulmonary veins may empty into the right side of the heart, into the persistent left superior vena cava, into the normal superior vena cava, or into the innominate or hepatic vein. Almost always there are cardiac anomalies associated with congenital abnormalities of the venae cavae and with the more important abnormalities of the pulmonary veins. Symptoms, signs, course, and prognosis depend on these other anomalies and not on the venous defects. The diagnosis of uncomplicated congenital defects of the great veins has now become possible in some cases by

means of cardiac catheterization and by detailed x-ray studies including angiocardiography

CONGENITAL ANOMALIES OF THE CORONARY VESSELS

Most anomalies of the coronary arteries and veins are of no clinical importance and are simply postmortem curiosities. These include extra coronary mouths (for example, the left circumflex coronary artery may arise directly from the aorta) one coronary mouth giving rise to both right and left coronary arteries, and unusual course and branching of the vessels. Rarely however a serious anomaly occurs this consists most frequently of the origin of the left coronary artery from the pulmonary artery which results in cardiac enlargement with hypertrophy and dilatation of the left ventricle, myocardial necrosis and fibrosis, and early death in the course of the first few months of life. One notable case was of a baby boy dying at the age of four months who suffered from attacks during life which closely resembled angina pectoris and showed an electrocardiogram with inverted ("coronary") *T* waves in Leads 1 and 2 (Bland, White, and Garland, 1933) Other cases have since been reported, one diagnosed antemortem (Eidlow and Mackenzie, 1946)

The most common important anomaly of the coronary veins is the persistence of the left superior vena cava (mentioned above) which takes the place of the coronary sinus this anomaly has, however no clinical significance. A very rare anomaly is the drainage of the coronary sinus into the left auricle.

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SEE ALSO GENERAL REFERENCES FOLLOWING CHAPTER 2 AND REFERENCES IN CHAPTERS 7 AND 9

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CHAPTER 14

RHEUMATIC HEART DISEASE

Introduction. Although at present apparently and happily on the decline, one of the three most common and serious types of heart disease is rheumatic; the other two are hypertensive and coronary The relative incidence of these types varies greatly in different parts of the world, in fact, in different parts of the United States of America for example, in New England more than twenty years ago the proportions were recorded as approximately 40, 29 and 36 per cent respectively with some overlapping of the latter two (White and Jones, 1928) in Virginia 22, 46 and 46 per cent respectively (Wood, Jones, and Kimbrough, 1926) in San Francisco somewhat more recently 22, 22, and 40 per cent respectively (Geiger et al. 1936) and in Texas 10 45 and 24 per cent for the whites and 4, 51 and 6 per cent for the Negroes (Stone and Vanzant, 1927) A reappraisal of these percentages is now in order because of the possibility of a changing incidence, as well as of more accurate statistics. Recent papers, for example, report 13.8 per cent among 436 cases of organic heart disease for Southwestern Virginia (Glendy 1948), 117 cases of rheumatic heart disease (11 per cent) as found among 1 045 cardiac autopsies in another southern group (Holoubeck and Holoubeck, 1947) and 26.9 per cent of 519 cardiacs in the Rocky Mountains (Cannon, 1946) A recent review of 3 000 cases of heart disease in New England (White, 1951) has given percentages of 23.5 26 2, and 48.5 respectively for rheumatic, hypertensive, and coronary heart disease. Thus climatic conditions and, to a much less extent, race have seemed to be important controlling factors, as will be noted in more detail later Other relationships that have become more and more evident in the past few decades are familial susceptibility social and economic status with particular reference to crowding, and the hemolytic streptococcus as an exciting factor these will be discussed shortly

One of the most important reasons why rheumatic heart disease is so serious is the fact that it is particularly a disease of youth, crippling and killing many children and young adults. As a result, many medical investigators and special

practitioners and social workers have undertaken campaigns to study the various problems involved and to reduce this menace and scourge which has assumed somewhat the role once held by the white plague, tuberculosis. During the fifteen year age period from 5 to 20 rheumatic fever with heart disease is, in the United States, the leading cause of death, and at ages 20 to 25 it is second only to tuberculosis (Armstrong and Wheatley *Studies in Rheumatic Fever* Metropolitan Life Insurance Company Nov 1944) In New York City in 1938 there were 1 105 deaths reported from rheumatic fever and rheumatic heart disease as compared with a combined total of 247 from whooping cough, meningitis, measles, diphtheria, scarlet fever and poliomyelitis (see Figure 81)

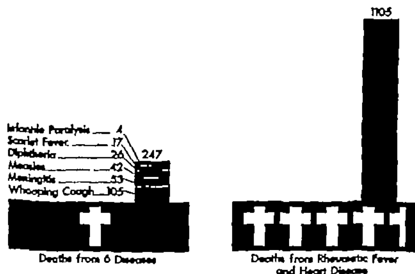


FIG. 81 Deaths from rheumatic fever and heart disease compared with deaths from six other common infectious diseases, New York City 1938. Data compiled by Dr Homer Swift. (Kindness of Dr David I. Rutstein and the American Public Health Association, New York.)

Already however either as the result of special efforts or because of an amelioration of the "rheumatic infection itself or both, or most likely of all, because of considerable improvement in living conditions there is some indication that in the last three decades (1920 to 1950) there has been a slight, but definite decline both in the severity and in the incidence of rheumatic heart disease (Hedley 1939 Wheatley 1949) evidences of which have been a drop from 27 cases per thousand patients in the wards of the Massachusetts General Hospital during the years from 1927 to 1930 to 22 cases per thousand during the years from 1937 to 1940 and finally 15 cases per thousand during the years from 1947 to 1950 a decrease from 16 cases per thousand at the Boston Floating Hospital in the years 1933 to 1937 to 9 per thousand from 1943 to 1947 and to 6 per thousand in 1948 and 1949 (kindness of Dr

James Baty) the complete clearing of a formerly long waiting list of children with rheumatic fever for admission to the House of the Good Samaritan in Boston, the decrease in rheumatic heart disease found recently in the school children of Denver Colorado, and a drop of relative incidence of rheumatic heart disease among cardiac admissions to the John Sealy Hospital in Galveston from 7 6 per cent in the decade 1920–1929 to 2.1 per cent in the decade 1930–1939 (Decherd and Herrmann, 1943)

The broad term "rheumatic heart disease" includes acute, subacute, and chronic involvement of the heart of the "rheumatic" type (as discussed under the heading Pathology to follow) whether or not a clear-cut history of rheumatic fever can be elicited. The rheumatic infection itself is manifested by a widespread reaction of the tissues throughout the body in this respect resembling tuberculosis and syphilis on the one hand, and allergy on the other In fact the terms "rheumatic granulomatosis," "the rheumatic state, and rheumaticosis have been suggested as better than the usual expressions "rheumatic polyarthritis," "rheumatic fever" and "the rheumati infection (Fahr 1929 Coburn, 1931 Graham, 1932)

Etiology *Cause* The cause of the rheumatic infection that plays such havoc in the heart is not yet clear It is the subject of intensive research at the present time and the solution of the problem is awaited with the keenest interest. Streptococci of various types have been considered in some way responsible for many years, and especially the hemolytic streptococcus (Coburn, and others) the general consensus of opinion is that the Streptococcus hemolyticus is the chief exciting factor which precipitates the so-called rheumatic state throughout the body particularly in the heart. Other exciting factors have, however been noted, such as typhoid vaccine (Bland and Jones, 1935) and even injuries, suggesting that the exciting factor is not specific nevertheless an acute streptococcus infection appears responsible in the vast majority of the cases. The finding of streptococci or other bacteria in the blood, joint fluid, or pericardial or pleural fluid of acute rheumatic cases has been occasionally reported but is not considered of primary importance, any more than the finding of immunologic reactions in tissues or blood. A decade or two ago a virus origin of the disease was suggested, but this has never been confirmed. Whether the tissue reactions throughout the body are due directly to bacterial toxin or result indirectly from an intermediary agent or as an allergic response has not yet been settled. Something akin to the last-mentioned hypothesis with particular involvement of the body s collagen is at present thought to be most likely but much research on this problem is in progress.

In recent years there have arisen interesting speculations concerning the possible role, in the production of rheumatic fever of the action of hyaluronidase, an enzyme, on hyaluronic acid a mucopolysaccharide, which with chondroitin sulfate is an important element in the ground substance of connective tissue, synovial fluid, and certain other parts of the body Certain strains of hemolytic streptococci produce hyaluronic acid and hyaluronidase and

salicylates have been reported to exert an antihyaluronidase effect. The possible etiologic relationships suggested by these findings and by the effects of hormones (ACTH and cortisone) need much further study before definite conclusions can be established.

Place of entry The place of entry of the rheumatic organism or virus (if such exists) into the body is probably the mouth. The faucial tonsils have been considered to be the chief portal, partly because their acute infection frequently ushers in acute rheumatic fever and partly because endocarditis may follow tonsillitis directly without any rheumatic symptoms. However other lymphoid tissue in the pharynx and nose may also harbor the "rheumatic" or activating organism and the gastrointestinal tract and foci of infection in sinuses and middle ear have not been ruled out as possible sources of "rheumatic" heart disease.

Rheumatic fever and chorea have been for many years regarded as the chief manifestations of the rheumatic infection that causes heart disease, but tonsillitis, "growing pains," and, in very young children, certain ill-defined fevers or illnesses have been thought to be allied as lesser and somewhat uncertain evidences of the same infection. The separation between these definite entities of rheumatic fever and chorea and the indefinite infections or symptoms mentioned, and between the latter and distinctly nonrheumatic diseases, is ill defined, in our present state of knowledge the borderline must be regarded as very wide Thus the diagnosis of a "rheumatic" infection, or of "rheumatic" endocarditis or heart disease, still often remains a matter of opinion. Two generations ago, as now it was rather the custom to consider all infectious heart disease in young people that was not of syphilitic or of "malignant" bacterial nature to be rheumatic in origin. One generation ago there arose the belief that "septic" infection of nonrheumatic type was frequently responsible when a rheumatic history was not obtainable. Probably the truth rests somewhere between these views, namely that the large majority of cases of infectious endocarditis are rheumatic in origin, but that some arise from other infections particularly terminal in nature, even when not of "malignant" bacterial type.

The more carefully one investigates the past history of patients with the rheumatic type of chronic heart disease, the more often one discovers a partly forgotten or mild rheumatism or chorea in such patients on the other hand, a prejudicial view is inclined to interpret every tonsillar infection or muscle ache as rheumatic. Furthermore, rheumatic fever does not frankly appear as such in the first few years of life, except in rare instances children affected with chronic endocarditis following some poorly defined illness in the second or third year of life are likely later to develop definite chorea or rheumatic fever with recurrent infection of the heart. It is safest to regard and to treat as rheumatic all infectious heart disease of childhood (unless it is "malignant" bacterial endocarditis) even though occasionally the cause is not clearly the rheumatic infection, the term "rheumatic type" of heart disease, acute, sub-

acute or chronic, covers satisfactorily for the present at least, the cases of doubtful etiology

A definite history of rheumatic fever mild or severe, can on careful investigation be found in 60 to 70 per cent of cases with "rheumatic" heart disease, and in another 5 to 10 per cent a history of chorea without rheumatism is obtainable. Chorea alone with no evidence of infection is not so often followed by heart damage (Jones and Bland, 1935) earlier opinions to the contrary were based on failure to exclude infection, particularly rheumatic fever

Sex Rheumatic heart disease attacks both sexes, but statistical analysis usually shows a more frequent incidence among females in the ratio of about 4 to 3 or 5 to 4 In one group of 956 cases there were 525 females and 431 males (White and Jones, 1928) and in another group of 1 000 cases studied at the House of the Good Samaritan in Boston there were 709 females and 291 males a 7 to 3 ratio, but the preponderance of beds available for females accounts partly for this high ratio (Jones and Bland, 1942)

Age In communities where rheumatic heart disease is common it is found in the great majority of cases between the ages of 4 years and 50 years. It rarely begins in the first four years of life, and is especially rare before the age of two years. A case of intrauterine rheumatic heart disease has, however, been reported (Kissane and Koons, 1933) also a case in an infant aged only 17 months has been noted (Schwarz, 1932)

Most recently a group of 26 very young children with active rheumatic fever has been reported by Logue and Hurst (1951) of these 26, 10 were under the age of four there being 3 three years old, 5 two years old, and 2 one year old there were also 9 who were four years old in this group, 6 who were five years old, and 1 whose exact age at the onset of rheumatic fever was not known but who was under five years of age. Despite such exceptions long experience has shown that as a rule rheumatic heart disease begins between the ages of 4 and 15 years with height of onset between the seventh and eighth years. It has been found that about 1 to 2 per cent of the school children in parts of the United States and Canada where rheumatic fever is prevalent have rheumatic heart disease, varying greatly however from place to place or from one part of a city to another (from less than 0.5 per cent up to 4 or 5 per cent) largely dependent on the degree of crowding of living conditions (Robey 1927 Keith and Pequegnat, 1947 Quinn, 1948) Although some cases develop relatively late, that is, after the twentieth year of life, this is distinctly unusual. The mortality beginning in the first decade, increases steadily and is highest in the second and fourth decades when infections (especially recurrent rheumatism) and heart failure take their toll. Occasional instances of survival to the age of 70 years, and a few even to 80 or over (White and Bland, 1941) are seen when the cardiac damage has not been extensive. The prevalence of rheumatic heart disease (*chronic as well as acute*) by decades in the New England group of 956 cases already noted (White and Jones, 1928) as compared with that of 684 cases analyzed 25 years later (White, 1951) was as follows

Race All civilized races and nationalities appear susceptible to rheumatic heart disease, although a somewhat lower incidence has been noted in China than in parts of Europe and America of the same latitude. In New England, people of English, Scotch, Irish, Scandinavian, French, Polish, Jewish, German, Italian, and Negro stock have all been found with rheumatic heart disease.

Table 6

AGE GROUPING OF CASES OF RHEUMATIC HEART DISEASE IN NEW ENGLAND

Years	*Group of 956 Cases Reported in 1928* Cases	Percentage	*Group of 684 Cases Reported in 1951* Cases	Percentage
0–10	116	12.1	53	7.7
10–20	299	31.3	223	32.6
20–30	135	14.1	71	10.4
30–40	165	17.3	91	13.3
40–50	123	12.9	102	14.9
50–60	78	8.2	89	13.0
60–70	35	3.6	38	5.6
Over 70	5	.5	17	2.5
Total	956		684	

Climate Climate appears to be an important factor in the incidence both of the rheumatic infection and of the rheumatic type of heart disease. The colder wetter parts of the temperate zone particularly favor these conditions, as do also the colder and wetter seasons of the year—winter and spring in New England, autumn and winter in old England. In the northern part of the United States the rheumatic infection and its permanent involvement of the heart are five times more frequent than in the southernmost part of the country or in the Philippine or Hawaiian Islands, while in the midzone the incidence is between these two extremes. For example, in Boston at the Peter Bent Brigham Hospital the incidence of rheumatic fever in the years 1914 to 1923 was 1.85 per cent of all medical admissions, the clinical incidence of mitral stenosis was 3.89 per cent, and the incidence of mitral stenosis in the autopsy room was 4.68 per cent, while in New Orleans at the Charity Hospital these percentages from 1916 to 1923 were 0.03, 0.08, and 0.23 respectively, and in Baltimore at the Johns Hopkins Hospital from 1914 to 1922, 0.73, 2.01, and 1.30 respectively (Harrison and Levine, 1924). This climatic difference has been so great that victims of the rheumatic infection have been advised sometimes to move from northern latitudes to southern and a few have done so; the reports from such a step have been in the main favorable (Coburn, 1931; Jones, White, Roche, Perdue, and Ryan, 1937), but it is to be noted that rheumatic heart disease has been discovered in recent years even in natives of tropical lands, such as Cuba (Perez de los Reyes, et al., 1944), Puerto Rico (Francisco, 1947), Panama (Hardgrove, et al., 1946), Curaçao (Hartz and Van der Sar, 1946), and New Guinea (Levine, 1946). Edström (1944) has even tried to influence the rheumatic infection by artificially producing a

tropical climate indoors in the temperate zone for long time treatment of active rheumatism with suggestive but not conclusive favorable results. The Rocky Mountain states harbor a considerable amount of rheumatic heart disease, up to 27 per cent of all cardiac patients (Cannon, 1946) as was confirmed by military experience during World War II while the high plateau, and perhaps even the lower lands also, in Mexico have shown a surprisingly great number of rheumatic heart cases, some 30 to 50 per cent of all cardiacs (Chavez, 1942 Cortes and Villarreal, 1947) It is likely that both prevalence of hemolytic streptococcus infection and overcrowded living quarters play an important role in these areas.

Family incidence One of the most interesting features of the rheumatic infection and of the rheumatic type of heart disease is their occurrence in different members of one family Several studies have indicated that from 32 to 50 per cent at least of patients with rheumatic fever chorea, or rheumatic heart disease have near relatives with a history of similar trouble (as compared to a control series) Three factors are probably responsible for such family incidence (1) inherited susceptibility to the rheumatic infection, (2) close contact, with the actual spread of the exciting organism from one throat to another and (3) crowded or unsanitary living conditions, sometimes with inadequate food and clothing.

Social and economic status An important factor in the occurrence of the rheumatic infection and of rheumatic heart disease appears to be the social and economic status of the individual. These diseases are much more common, by 100 per cent at least, among the crowded poor than among the well-to-do inhabitants of almost every community In the large American private schools rheumatic fever chorea, and rheumatic heart disease are infrequent, while in the large public schools they are relatively common. Crowding, exposure to cold and wet without sufficient protection, malnutrition, and fatigue are probably all factors in producing this contrast.

Epidemic form. Finally there is some evidence that at times under suitable conditions the rheumatic infection, in the nature of rheumatic fever assumes an epidemic form This was noted among the soldiers during World War I and infrequently among civilians since, and was encountered again in World War II It may occur when an infecting organism of unusual virulence attacks a group of susceptible individuals exposed to adverse conditions, such as bad weather and fatigue. It has been especially noted in groups of young people immediately following infection by a virulent hemolytic streptococcus in epidemic form a certain number of "susceptible" individuals, though a small percentage of the persons attacked by the original infection, may develop rheumatic fever In camp barracks and other living quarters of military personnel during World War II about 4 to 5 per cent of the young men exposed to and infected by the hemolytic streptococcus of various strains developed rheumatic fever some 10 to 15 days later this was especially noted among the new recruits and in more crowded living conditions and in colder climates (Feasby 1944 and Barber 1946)

Pathology A generation ago endocarditis was the only well-recognized common manifestation of rheumatic heart disease, acute or chronic; pericarditis was admitted as an occasional complication, but little attention was paid to involvement of the myocardium or as a matter of fact, to the wide spread effects of the disease throughout the body Much advance in the proper understanding of this kind of heart disease has come in the last thirty years.

The more severe the rheumatic infection in early youth, the more extensive as a rule is the cardiac damage. Once it was thought that only about two thirds of the attacks of rheumatic fever and about one third of those of chorea affected the heart, but careful examination is now revealing a somewhat different incidence. There was, for example, evidence of permanent cardiac damage in 86 per cent of 518 cases of rheumatic fever in 73 per cent of 348 cases of chorea and rheumatic fever and in 3 per cent of 134 cases of uncomplicated chorea analyzed at the House of the Good Samaritan in Boston (Jones and Bland, 1935) Findings vary however as indicated by another series of 175 cases of acute rheumatic fever 50 per cent of whom showed no evidence of heart disease after follow-up periods averaging seven years (Brown and Wolff, 1940) Electrocardiographic and postmortem examinations have often shown myocardial and even slight endocardial involvement even though on physical examination there had been no sign whatsoever of heart disease. It is probable that in every case of rheumatic infection there is some heart disease however slight or transient, and that in a certain percentage of the total number there is complete recovery with return to normal, or at least not sufficient deformity of valves or lesion of myocardium or pericardium to produce abnormal signs.

The typical heart lesion of the rheumatic infection is an inflammatory reaction about the smaller arteries, consisting of groups of small round mononuclear cells with a few giant cells (Aschoff, 1904) this has been called the Aschoff body (Figure 82) and its discovery anywhere in the heart or pericardium has been considered almost pathognomonic of the activity of the rheumatic infection. There may be but few of such lesions present or they may be widespread and in groups. They apparently come and go, leaving no trace, unless the disease has been so extensive that nutrition has been interfered with and scar tissue results a sequela of more than slight fibrosis is very rare in the myocardium, although a few instances have been recorded of rheumatic heart block remaining as a chronic state after it has appeared during the acute rheumatic infection.

Aschoff, L. "Zur Myocarditisfrage. *Verhandl d deutsch. path. Gesellschaft* 1904 VIII, 46.

Aschoff here gives the first clear description of the more or less specific rheumatic myocardial lesion which has been called by his name (Aschoff body) (The translation is by myself.)

"W have succeeded in establishing the histological structure of the myocardial reaction to the rheumatic infection by finding peculiar nodules which appear to be specific. These nodules were indeed clearly defined in only two cases of recurrent endocarditis, but in other cases cellular proliferations corresponded exactly in

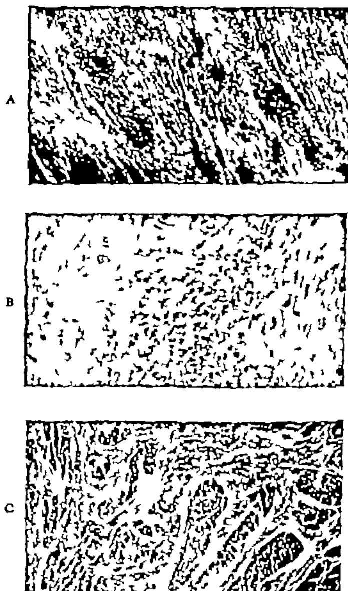


FIG. 84. Rheumatic myocarditis. (*A*) Microphotograph showing typical Aschoff bodies in the (ventricular) heart muscle in acute rheumatic heart disease. (Thalhimer and Rothschild, *J Exper Med* 1914 XIX, 417.)

(*B*) Microphotograph (higher power) of myocardium of child dying of severe rheumatic infection showing extensive destruction of the muscle cells with infiltration by leukocytes and a few multinucleated giant cells. (Kindness of the House of the Good Samaritan, Boston.)

(C) Microphotograph of myocardium from case dying of severe recurrent rheumatism. There is evident at the left old fibrotic change from a previous rheumatic infection, and at the right new necrotic and hemorrhagic lesions due to the recurrent rheumatism. (Kindness of the House of the Good Samaritan, Boston.)

their locations to the lesions of these two hearts. They were regularly situated in the neighborhood of the small and medium sized blood vessels and often showed the closest relationship to the adventitia of these vessels. There even was found a disease of all the vessel walls somewhat comparable to that described for arteritis nodosa. The above mentioned nodules are extraordinarily small, highly submiliary and are comprised of collections of unusually large cells with one or more abnormally large, slightly notched or polymorphic nuclei. The grouping of cells often occurs in the form of a fan or a rosette. The periphery of the nodule is composed of the large nucleated cells and the center often of an apparently weakly staining necrotic mass of coalescent cellular protoplasm. With careful observation the fan-shaped foci remind one of the smallest necrotic areas with cellular periphery which one finds so often in gouty kidneys. In the rheumatic nodules one has to do not with the tubercular or foreign body giant cells with several regularly formed nuclei, but with structures which resemble rather the large nucleated cells in certain sarcomas or in pseudoleukemic proliferations. On the other hand the nodules are not composed solely of such large-nucleated cells, but small and large lymphocytes and also polymorphonuclear leukocytes are wedged in between the large cells, at least at the periphery or else themselves comprise an outer zone from which irregular stray cells extend out further into the connective tissue interspaces. In these outer areas there can still be found single large nucleated cells and all gradations down to simple large leukocytic elements which are more or less commonly found in the neighborhood of the smallest vessels in all inflammatory reactions. These leukocytic elements are the large cells, which Hayem and Romberg have described but whose origin remained doubtful in their minds. Out of these large cells, which are the adventitial cells of the blood vessels swollen by inflammatory reaction, the large-nucleated giant like cells are formed, which, single or collected in nodules, give to the rheumatic proliferations a characteristic stamp. It should further be observed that the number of eosinophilic cells in these nodules is very small.

Years later it was demonstrated that the Aschoff body is not the earliest tissue change in the rheumatic infection but often is a rather late reaction, probably a part of the process of recovery and repair (Coburn, 1933). The earliest tissue changes are those of destruction (necrosis) and a tendency to hemorrhage throughout the body, especially well marked in the more severe cases. The myocardium particularly is involved and may be so seriously damaged in the sicker children that the heart dilates acutely or subacutely. Such dilatation of the heart may lead to death from heart failure or to more or less permanent cardiac enlargement, or it may be followed by good recovery with more or less complete return of the heart to normal size. *The recognition of this fact is of the greatest importance* in the proper understanding of the cardiac symptoms and signs in the course of the acute and subacute rheumatic infection, in the analysis of the late after-effects, and in rational prognosis and treatment.

The typical rheumatic endocarditis consists of a so-called verrucous inflammatory reaction, tiny vegetations of thrombotic nature composed chiefly of fibrin and tending particularly to appear in a row on the atrial surface of the mitral and tricuspid valve cusps and on the ventricular surface of the semilunar valve cusps (Figure 83) at the line of closure, not at the edge, although

sometimes they are distributed elsewhere over the cusps. The exact pathogenesis of these thrombi or of the damaged areas of the endocardium on which the thrombus formation takes place is not known, whether due to direct toxic action of the blood stream, or via the blood vessels in the valves, or to local allergic reaction to agent or agents in the blood (manufactured elsewhere). In any event the slight trauma caused by valve closure appears of some importance in favoring the appearance of the earliest lesions. In fact nonrheumatic



FIG. 83 *Photograph showing acute and chronic rheumatic endocarditis of the aortic valve.* Note the vegetations along the line of closure, adhesions of the cusps, to produce slight aortic stenosis, scarring of the endocardium below the valve, and thickening of the chordae tendineae of the mitral valve. The patient was a boy 14 years old. (Kindness of Dr Ronald Grant, Guy's Hospital, London.)

bland thrombi of small size very probably are deposited on the lines of closure of the heart valves, especially the mitral, on occasion almost as a normal event, the result of a variety of influences they may do no serious harm but can quite likely result in a slight chronic thickening of the valve edge which may justifiably or not, arouse suspicion of a rheumatic etiology Besides the involvement of valve cusps there is commonly in rheumatic endocarditis, especially of the severe type, inflammation of the chordae tendineae and of the wall of ventricle or atrium, especially of the left atrium just above the valve: this results in scarring and, in the case of the chordae, in thickening, shortening, and coalescence to add to the valve deformity

Rheumatic pericarditis consists of a fibrinous or a serofibrinous reaction, more or less extensive, sometimes giving rise to the typical bread and butter appearance (as shown in Figure 134 page 710) but rarely to large effusions (a typical serous exudate, rarely bloody) In healing, small or large scars are left with or without localized or complete adhesions, and only rarely with any important external adhesions. Constrictive pericarditis of sufficient degree to cause symptoms or signs (Pick's disease) has not been encountered once in 1,000 cases of the rheumatic infection, many with pericarditis, followed over a ten to twenty year period at the House of the Good Samaritan in Boston (Jones and Bland, 1942) nor has any one of 53 cases of chronic constrictive pericarditis examined by myself had a rheumatic etiology although two among them had coincidental rheumatic valvular disease.

When, as frequently happens, myocardium, endocardium, and pericardium are all involved we speak of *pancarditis* and now and then, especially in young children, such pancarditis may be very severe and overwhelming, resulting in early death from heart failure.

Furthermore, the rheumatic infection may attack other organs beside the heart, pericardium, joints, and brain (chorea) The arteries—aorta, pulmonary artery and smaller visceral and peripheral vessels—the lungs, the pleurae, the diaphragm, and the peritoneum may be involved by hemorrhages or by lesions resembling the Aschoff body sometimes with serious consequences. An important and interesting pulmonary rheumatic lesion in severe cases is the hemorrhagic consolidation, sometimes labeled erroneously rheumatic pneumonia, this lesion quickly comes and goes.

The rheumatic infection is typically a slow one and recurrent, a fresh invasion of the heart is common on top of healed lesions of valves or of atrial or ventricular endocardium, of chordae tendineae or of pericardium.

The infection may clear up in some cases, as stated above, with little or no trace, but commonly a scarring of the endocardium is made evident by valvular deformity Chronic pericardial damage sometimes persists in the nature of adhesions of varying extent and importance. Rarely there is a residual myocardial lesion as shown by permanent heart block or ventricular dilatation. A discussion of the particular valve lesions, of pericarditis, and of heart block will be found in Parts III and IV of this book. Suffice it to say here that there is a very wide variation of cardiac damage resulting from the rheumatic infec

tion and constituting chronic rheumatic heart disease, not only with respect to the particular parts of the heart involved but also with respect to the degree of involvement.

It should be added that chronic cardiac dilatation accompanying valvular defects or pericardial adhesions may be due as much or more to the rheumatic infection of the myocardium as to the particular valvular handicaps that cause heart strain. Indeed it may be conjectured that in rare cases cardiac enlargement, even of high degree and leading to failure, may be due to an old severe antecedent rheumatic involvement of the myocardium with little or no endocardial or pericardial scarring. This is an explanation of some of the cases of heart disease of unknown origin which appeals to one as logical but which as yet lacks proof.

Symptoms. The symptoms of rheumatic heart disease depend upon three factors (1) activity of the rheumatic infection, (2) obstruction to the circulation resulting from the specific lesions, and (3) heart failure which may come as the result of overwhelming acute or subacute myocarditis, or of chronic valvular disease, or of disturbed heart rhythm, or of two or even all three of these conditions combined. Many persons with chronic rheumatic heart disease have no symptoms at all and live active lives without difficulty Of greater immediate importance than study of the structural defects is the determination of the presence or absence of activity of the rheumatic infection.

The symptoms of acute or subacute rheumatic infection include those of any infection but depend also on the reaction of the individual patient to the causative agent. Joint pain, tenderness, swelling, heat and redness, muscle aching, chorea (rarely combined with joint symptoms) fever chills (rarely) sweating (sometimes profuse) weakness, effort syndrome, malaise, anorexia, epistaxis (occasionally) and loss of color and weight are all symptoms of the active rheumatic infection. Their severity varies with the virulence of the infection and the resistance of the patient. They may be mild and hardly noticeable —merely slight fever and malaise with or without muscle or joint soreness— and not always sufficient to cause the victim to stop school or work or to induce the family to consult a physician unless they have been educated by previous experience or are aware of the likelihood of involvement of the heart. In rare cases of rheumatic fever there may be abdominal pain simulating that of or actually due to, an acute appendicitis. A low-grade rheumatic heart infection, ordinarily called subacute rheumatic carditis, may set in and last for weeks or months, or even years, especially in children, showing itself only by a loss of energy and by the appearance of ill health and of a slight elevation of temperature at intervals or daily (99 F or a little more by mouth, or 100 F by rectum) Such a situation is very common, while a virulent polyarthritis in children is relatively rare. A severe short attack of rheumatic fever with extreme joint involvement and little or no heart disease is much more likely to occur in the adult. Years ago it was a common though by no means invariable rule that the older the individual, the more the joints suffered and the less the heart; the younger the subject, the more the heart suffered and

the less the joints. In recent years, on the other hand, a fulminating polyarticular rheumatism is rarely seen at any age even in New England this is apparently due to a spontaneous change in the virulence or character of the rheumatic infection itself, though the common and early use of the salicylates (especially aspirin) for any illness by the populace at large may also have a modifying and misleading influence on the acute rheumatic process.

The heart itself when acutely invaded by the rheumatic infection, only occasionally causes symptoms. Sometimes it may ache so that precordial discomfort is felt, sometimes there are sharp pains in the chest, although they are not common rarely there is actual angina pectoris, occurring usually in subacute or chronic valvular disease with marked aortic regurgitation, probably dependent on insufficient coronary blood supply due not only to low diastolic blood pressure but also to a storm of vasoconstriction involving the coronary arteries and producing transient hypertension in a sensitive individual. Infrequently disturbances of rhythm occur such as premature beats or paroxysmal tachycardia, giving rise to palpitation usually the palpitation that may be felt is but a part of the effort syndrome that accompanies any infection. Dyspnea also is usually due to effort syndrome, but sometimes it arises from an acute pericarditis or from cardiac dilatation and failure accompanying an overwhelming acute myocarditis. When the heart fails during the acute rheumatic infection in childhood, it is a total heart failure with little or no dyspnea but with congestion behind the right ventricle giving rise on occasion to upper abdominal discomfort from engorgement of liver and other abdominal viscera.

The chronic rheumatic heart frequently fails from the strain of valvular disease complicated by a disturbing arrhythmia (especially atrial fibrillation) or by an acute infection (rheumatic or nonrheumatic) then appear the typical symptoms of congestive failure (see Chapter 30) Angina pectoris may occur with marked aortic stenosis or regurgitation but rarely with other valve defect. Also, without actual failure, the obstruction due to mitral stenosis may occasion congestion of the lungs with dyspnea, cough, hemoptysis, or it may rarely cause hoarseness from laryngeal paralysis At times the obstruction due to tricuspid stenosis may block the return of blood into the right ventricle and left heart chambers with resulting congestion of liver and large veins, similar to the condition found in cases of chronic constrictive pericarditis (so-called Pick's disease)

The symptoms of an active rheumatic infection may frequently be superimposed on those of chronic rheumatic heart disease when there is a recurrent rheumatic attack In fact, heart failure in chronic rheumatic heart disease is often precipitated by the new infection or is due more to its presence than to the old lesion.

Signs. The signs of rheumatic heart disease are dependent on the factors of activity of the infection, of the strength of the heart, and of the particular lesions. There may be nothing but slight enlargement of the heart with a systolic murmur at the apex or a slight diastolic murmur along the left border

of the sternum found on routine examination there may be an enormously enlarged heart with several murmurs, absolute arrhythmia, and marked congestive failure· or there may be any combination of signs between these two extremes. Commonly in the child there is slight to moderate cardiac enlargement with normal rhythm moderate systolic and middiastolic murmurs at the apex (the result of left ventricular dilatation during the course of the first rheumatic infection and, later on, of mitral valve disease itself) and sometimes a diastolic blow (of aortic regurgitation) along the left border of the sternum, without frank congestive heart failure, but frequently with slight fever due to activity of the rheumatic infection. It is a common experience to note the disappearance of the physical signs of rheumatic heart disease (enlargement, systolic murmur and even mitral diastolic murmur) when cardiac dilatation subsides along with the active rheumatic infection (Bland, Jones, and White, 1936) these signs, especially the mitral diastolic murmur used to be attributed to chronic heart disease, but now it is realized that usually an interval of several years is necessary for the establishment of structural mitral stenosis. Commonly in the adult, on the other hand, especially in the female, there is a well-marked apical diastolic murmur of mitral stenosis, absolute arrhythmia of atrial fibrillation, and very limited cardiac reserve or slight to moderate congestive failure, with or without aortic regurgitation in the adult male one finds somewhat more often a preponderant or even seemingly isolated aortic valve lesion (stenosis, regurgitation, or both) with normal rhythm. Although these findings are the most common, they may be replaced by others. The signs of the particular valve defects will be discussed in Part III.

The more severe cases of active rheumatic infection may show also frank congestive heart failure, which in childhood involves the whole heart with resultant systemic venous congestion (big liver and dependent edema, including the face with the child lying flat) rather than pulmonary congestion due to primary left heart failure (Walsh and Sprague, 1941)

Infrequently one finds in acute rheumatism two additional signs, which are subcutaneous and cutaneous manifestations rheumatic nodules and skin lesions.

Rheumatic nodules are important signs of a severe rheumatic infection; their presence indicates that the infection is still active even though they persist or recur for many months. These nodules vary in size, number location, and with the severity of the disease. Usually of pinhead to pea size and shape, rarely as large as Lima beans, they are found most commonly subcutaneously and are loosely attached to tendon sheath, periosteum, or joint capsule over elbows, knees, ankles, skull, fingers, wrists, toes and shoulders, in frequency in about the order named, and usually more or less symmetrically on the two sides of the body (Figure 84) When very extensive they may be found scattered over the entire head, thorax, and long bones. In number they vary from two or three, a common finding, to one hundred or more, very rarely They tend to come and go singly or in crops, each one lasting for a few days or weeks they may not completely disappear for months. In some parts of the

world they are more common than in others, but this variation is probably due mainly to the severity of the infection. Their incidence has extended from 2 or 3 per cent to over 75 per cent in different groups of patients with acute rheumatic infections in different communities. They are less commonly seen nowadays in New England than they were two or three decades ago, perhaps paralleling the decrease in the severity of the disease itself

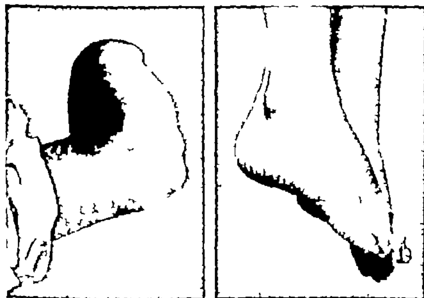


FIG. 84 Photograph showing joints of child with rheumatic nodules on elbow ankle, and foot. Note nodule also on the tendo Achillis. (Kindness of the Cardiac Clinic, Children's Hospital, Boston.)

Erythema multiforme (marginatum) is the commonest of the cutaneous signs accompanying the rheumatic infection, occurring in about 15 per cent of the cases at some time or other tending to recur over periods of a few weeks or months and to appear in patients who have had or who later develop rheumatic nodules. Erythema nodosum, urticaria, and angioneurotic edema are relatively rare. Purpura rheumatica and petechial hemorrhages are sometimes found. Petechiae may be readily produced in the skin of subjects with an acute or subacute rheumatic infection by pressure, as with a blood pressure cuff, this is due to the tendency to bleed which is a part of rheumatic fever as well as of bacterial endocarditis.

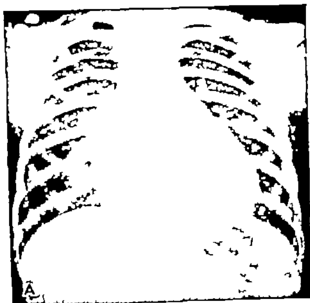
Other occasional signs of severe rheumatic infection are those of acute pleuritis, acute pericarditis, or both, fibrinous or with effusion, and sometimes hemorrhagic pulmonary disease (areas of hemorrhagic consolidation) which are apparently of rheumatic origin and as a rule rapid in their appearance and disappearance. Chronic adhesive pericarditis may show itself in the recovered cases but often it gives no clear sign. This will be further discussed in Part III of this book.

The results of all other methods of examination of an individual with rheumatic heart disease are likewise dependent on the three factors of activity of infection, cardiac insufficiency and the particular structural lesion. Commonly it is the presence of mitral valve disease and of stenosis of that valve that accounts for the findings in chronic cases.

The blood pressure is normal or low unless there is a complicating essential hypertension, thyrotoxicosis, or considerable aortic regurgitation. The pulse and pulse pressure are very full when there is marked aortic regurgitation, small when there is considerable mitral stenosis, and very small when there is pronounced aortic stenosis.

Roentgenologic study is of help in following a case of rheumatic heart disease. In the acute infection and early stages of organic involvement the heart shadow may be normal, or it may reveal enlargement and change in shape of the heart shadow due most often to more or less acute dilatation of the heart (Figure 85) or less commonly to accumulation of fluid in the pericardium in rheumatic pericarditis, or to both of these conditions. In chronic cases it shows various typical changes of shape and size when there are well-marked chronic valvular lesions (see Chapter 26)

The electrocardiogram may be normal in rheumatic heart disease except for a rapid rate (sinoatrial tachycardia) which is found frequently but if many serial records are taken of any case, abnormalities are commonly found, though often in but a few records. When the electrocardiogram is abnormal it may show either an arrhythmia, delay in conduction between atria and ventricles abnormal *T* waves, intraventricular block, or abnormal axis deviation. The rhythm is absolutely irregular in more than half of the adult cases with marked mitral stenosis, but it is generally normal or disturbed only by premature beats in aortic valve disease pericarditis, or preponderant mitral regurgitation. Slight grades of heart block as shown by *P-R* intervals of 0.21 or 0.22 second are common during the acute rheumatic infection (Figure 86) and even *P R* interval prolongation to 0.25 second, dropped beats, or higher grades of block are occasionally seen. This finding of block may be the only sign of cardiac involvement and it has been noted in rare cases as the first evidence of the rheumatic infection in the body polyarthritis developing shortly afterward (White, 1916) Also in very rare cases the heart block during the active infection may progress to such a high degree that Adams-Stokes attacks occur for a short time. As a rule the heart block clears up when the rheumatic infection subsides, but a few instances of permanent rheumatic heart block have been noted, and it has also been observed that rheumatic heart cases with a persistently prolonged *P-R* interval are more likely to develop atrial fibrillation than are those whose *P-R* interval is normal, due in part, it is suggested, to vagal action (Bruenn, 1937 Altschule 1939) It is important to note moreover that prolongation and variability of the *P R* interval can occur in normal children, as well as in rheumatic children without evidence of rheumatic activity (Reyersbach and Kuttner 1940)



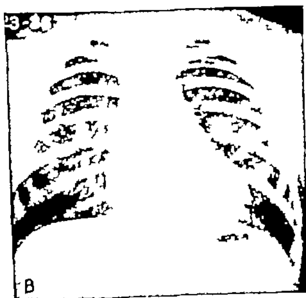


FIG. 85 Roentgenograms showing (*A*) considerable dilatation of the heart in young girl during acute rheumatic fever and (*B*) reduction in heart size several months later after complete subsidence of the infection. At the time the first record was taken there were systolic and middiastolic murmurs at the apex which disappeared when the dilatation subsided. There was no evidence of acute pericarditis. Note the rather localized pulmonary edema in the right lung in (*A*). The transverse diameter of the heart in (*A*) was 11.6 cm and in (*B*) 10.4 cm.

In addition to the delay in atrioventricular conduction, slight deformities of the QRS and T waves or of the S-T segment are occasionally noted during the acute and subacute infection and may represent slight transient intraventricular block, myocarditis, and pericarditis rarely they may persist. In a few cases of chronic rheumatic heart disease, particularly with mitral stenosis, bundle branch block of the right type, with wide S_1 or QS_1, may be

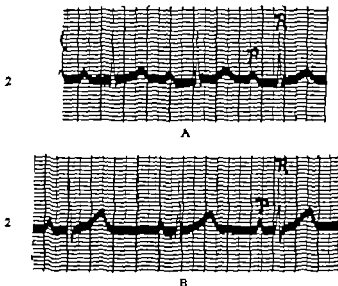


FIG. 86. Electrocardiograms showing Lead in (*A*) during acute rheumatic fever Dec. 17 1935 and in (*B*) two weeks later during convalescence, Jan. 2, 1936. Note the prolonged *P-R* interval (0.25 second) in (*A*) and normal *P-R* interval (0.17 second) in (*B*) Boy 13 years old. Time = 0.1 and 0.2 second.

found. Finally it is common to find abnormal axis deviation and ventricular preponderance *in chronic valvular disease* if either mitral stenosis or aortic regurgitation is preponderant and of marked degree, right axis deviation occurring with the former and left axis deviation with the latter Absence of abnormal axis deviation by no means rules out either valvular lesion In fact high degrees of both may be present in the same case with normal electric axis deviation, the effect of involvement of one of the valves neutralizing the effect of involvement of the other in the classical limb leads, but the precordial leads reveal the enlargement of both ventricles. A very interesting electrocardiographic finding occasionally seen in acute rheumatic fever with congestive heart failure is a shift of the electric axis to the right due, doubtless, in large part to the acute right ventricular dilatation (more marked than that on the left side) which decreases or disappears with the patient's improvement or recovery (Walsh and Sprague 1941) Prolongation of the Q T time has been reported in rheumatic fever but it is not a consistent finding and may be due to other factors (e.g. cardiac enlargement) rather than to the rheumatic fever itself

Blood and urine are frequently abnormal when there is an active rheumatic, or complicating, infection or congestive failure. A leukocytosis of 10 000 or over often, but not always, accompanies acute rheumatic heart disease the severer the infection, the higher the white count, but it rarely passes 20 000. A slight or even moderately severe hypochromic anemia is common in children with active rheumatic heart disease. The sedimentation rate of the blood is usually increased in proportion to the activity of the rheumatic disease and may be the only evidence that persists of a long-drawn-out low grade infection. The blood culture is usually negative. A positive skin reaction has been reported as a frequent finding when the toxic filtrate of the hemolytic streptococcus (or its nucleoprotein) is injected intradermally in patients who have had rheumatic fever but this has been found to be a nonspecific reaction, that is, it occurs also in cases who have had Streptococcus hemolyticus infections without rheumatic fever Albuminuria is the usual finding during congestive heart failure and during moderate or high fever in the acute rheumatic infection. Occasional red blood corpuscles are frequently found in the urinary sediment during the active infection.

Course and prognosis. Rheumatic heart disease begins with an acute invasion of the heart, generally in childhood between the ages of 4 and 12 years. Instances of very early infection are on record, even in the fetus and in the nursing infant whose mothers had rheumatic fever at the time· on the other hand, the rheumatic infection and resulting heart disease have sometimes occurred first in adult life initial attacks of rheumatic fever have been reported in six patients over 60 years of age (Ferris and Myers, 1935) I have myself encountered cases with recurrent attacks at 66 and at 72 years of age. The earlier in life the cardiac involvement, the more serious it is likely to be and the shorter the patient's life. It is usual for the child to survive the first rheumatic infection, whether it is frank rheumatic fever chorea, ill-defined sickness, or rheumatic heart infection alone. Although this earliest infection is often mild it may last for months or years and leave a badly crippled heart. Recurrent infections throughout childhood may cause death by heart failure, by the toxic effect of the disease itself, or by complications. But usually there is survival in spite of one, two three, or more fresh attacks or exacerbations of rheumatism in childhood and youth, the victim showing a variable amount of permanent heart damage by the time he reaches the age of 20 years. Rarely does he escape unscathed, unless he has had but one or at most two slight attacks of rheumatism. The greater the number of recurrences of the infection, the greater is the heart damage. In adult life he runs far less risk from new rheumatic attacks, but on the other hand he runs three other risks (1) atrial fibrillation, (2) congestive heart failure, and (3) subacute bacterial (Streptococcus viridans) endocarditis. The first of these complications (atrial fibrillation) is common in the case of well-marked mitral stenosis but it is relatively rare in all other cases. The second (congestive failure) is likely to occur in any severely damaged heart when there is aortic or mitral valve disease, uncontrolled tachycardia (especially in atrial fibrillation)

infection, rheumatic or otherwise, which adds appreciably to the strain. The third (subacute bacterial endocarditis) is commonest in aortic valve disease or with mitral lesions in which stenosis is not marked, that is, when regurgitation predominates so it is most common in just that type of chronic rheumatic heart disease which atrial fibrillation and congestive failure are not likely to accompany but why this should be so we do not yet know

Death from heart failure or complicating infection commonly overtakes the victim of rheumatic heart disease in the second, fourth, or fifth decade of life, after many years, usually ten to twenty of partial crippling and restriction of activity and after a few years, usually two to five, of partial or complete invalidism. Sometimes, however if the lesions are but slight and the subject is careful, fortunate, or both, he may survive to old age and die a noncardiac death. Slight mitral stenosis or regurgitation, slight aortic stenosis or regurgitation, and a noncrippling adhesive pericarditis are all lesions that are well borne with respect both to duration and to activity of life, but in general the mitral valve lesions are better borne than the aortic. A ten year follow-up of 506 cases with rheumatic valvular lesions gave a relative mortality of 3 7 per cent for mitral insufficiency 12.5 per cent for mitral stenosis, and 37 4 per cent for aortic valve lesions with or without mitral valve involvement (Svartz and Ernberg, 1947) In Texas, Fashena (1944) found the death rate from rheumatic fever in the school age period to be not very different from that in New England or in the United States as a whole Cases of mitral stenosis surviving the age of 80 years are now on record (White and Bland, 1941) Wilson and Lubschez (1948) have presented some interesting data as to longevity based on a thirty year period of observation of 1 042 children who had rheumatic fever The mean age at onset of their rheumatism was 6.5 years. The average length of observation was 14 8 years among 226 deaths 75 7 per cent were due to rheumatic disease of the heart and 10.2 per cent to subacute bacterial endocarditis. They concluded that an affected child has 4 chances out of 5 to survive childhood, 3 out of 4 to survive puberty and then 19 chances out of 20 to survive early adult life, with an overall chance of 1 out of 2 to survive the age of 40 years.

Complications. The three most important complications of rheumatic heart disease have been mentioned above (1) atrial fibrillation which complicates two thirds of the cases of considerable mitral stenosis and about one fifth of all cases of chronic rheumatic heart disease (17.5 per cent of the 956 cases of White and Jones series) (2) congestive heart failure which eventually complicates at least two thirds of all cases, and (3) subacute bacterial (Streptococcus viridans) endocarditis which attacks one in every 4 to 20 cases (25 to 5 per cent) of rheumatic heart involvement. Jones and Bland (1942) have found subacute bacterial endocarditis in 16 (7 9 per cent) of 203 fatal cases of rheumatic fever or rheumatic heart disease, while Gelfman (1943) has reported the finding of such involvement in 25 [illegible] cent of autopsied cases of rheumatic heart disease in two Boston hos[illegible] common or important complications are co[illegible] disease [illegible] of White and Jones

series) essential hypertension (also in 2 per cent of White and Jones series) syphilitic aortitis, congenital defects, thyrotoxicosis, and emphysema (each of which last-named conditions complicated less than 1 per cent of White and Jones series) Neurocirculatory asthenia frequently is found in varying degree in the victim of rheumatic heart disease it was well marked in 37 of the 956 cases (4 per cent) of the series noted above (White and Jones) Mild and serious infections of all sorts, nephritis, pulmonary disease, nervous diseases, and lesions of the gastrointestinal tract may complicate rheumatic heart disease, but it is of interest to note that glomerulonephritis rarely accompanies rheumatic fever itself (Baehr and Schifrin, 1931) The relative infrequency of pulmonary tuberculosis in cases of well-marked mitral stenosis has been pointed out; it has been suggested that the chronic pulmonary stasis in mitral stenosis protects the lungs from tuberculosis.

Four complications of rheumatic heart disease are largely dependent on the mitral stenosis or congestive failure that may be present. The commonest is pulmonary embolism which may arise in dilated right heart chambers but most often comes from thrombosed veins in legs resulting largely from the venous stasis secondary to the heart trouble. Embolism to brain or elsewhere may result from thrombosis in the left atrium. Acute pulmonary congestion producing edema or hemoptysis may come from increased pressure in the pulmonary circulation due to mitral stenosis, especially when there is a rapid heart rate. Rarely hoarseness may result from left recurrent laryngeal paralysis.

Another rare complication, namely that of angina pectoris, may attend rheumatic heart disease· It was found in 13 of White and Jones series of 956 cases, the 5 older cases having coronary disease and the 8 younger ones marked aortic regurgitation. Angina pectoris may also very rarely complicate mitral stenosis in young people (Hochrein, 1930)

Of disturbances of rhythm atrial fibrillation and heart block have been discussed. Atrial flutter is rare, generally complicating mitral stenosis. Paroxysmal tachycardia (regular) is common, but less frequent than atrial fibrillation. The presence of sinus arrhythmia, although somewhat favorable, is of little aid in the judgment of a case, since it does not indicate that the heart is normal and since it does not prove that a low-grade active infection is no longer in progress, as was once thought.

Treatment. No treatment for rheumatic heart disease per se is needed unless one or more of the important complications are present—infection, atrial fibrillation or flutter or congestive failure. The treatment of the arrhythmias and of congestive failure is discussed in Part IV of this book. In prevention of acute rheumatism, either in first or in recurrent attacks, the most important measure is the avoidance of upper respiratory infections or the early and adequate use of penicillin if the hemolytic streptococcus is the offending agent. Although helpful it is not essential to enlist the aid of a mild climate for children have been kept well even in open-air sanatoria in the north in the winter by practical exclusion of infected contacts (Hubbard and Griffin, 1940)

If acute or subacute rheumatic infection is present, *rest in bed* a light simple diet with adequate vitamins, and appropriate therapy directed against the infection are indicated. Usually *good nursing care* is of prime importance and worth more than most drugs. Satisfactory gain in weight is a good indication of the favorable progress of convalescence, but it is not a sign of cure.

In the third edition of this book it was stated that "for the rheumatic infection itself no specific therapy has as yet been established although much reliance has been placed by some on the *salicylates* which, without any question, have a well-nigh specific effect in the rapid control of fever joint swelling, and pain in rheumatic fever for which purpose they may be freely used. It is possible also, though not proved, that salicylate therapy may help to effect a rapid absorption of rheumatic pericardial and pleural exudate and effusion." Since that time hormone therapy of arthritis and certain other diseases, including rheumatic fever has been introduced, which may or may not prove to be specific or very near it.

Hormone therapy The application of ACTH (adrenocorticotropic hormone) to acute rheumatic fever has been tried recently with surprising immediate success in the majority of cases, for example, seven patients at the House of the Good Samaritan in Boston given 10 to 25 mg of ACTH four times a day for four to six weeks have all responded favorably As a rule, their temperature has been reduced to normal in two to three days, their sedimentation rates have become normal in two weeks, and even those seriously ill with congestive failure have improved greatly although they still may need other treatment for the congestion itself. Cortisone also has been found to be effective in suppressing the disease (Hench, et al., 1950) These preliminary observations, of course need further confirmation and more prolonged follow-up

Salicylate therapy A dose of 15 to 30 gr (1 to 2 gm) of sodium salicylate with an equal amount of sodium bicarbonate every two to four hours until relief of symptoms and of fever or a toxic reaction (tinnitus, nausea, vomiting, urticaria) has ensued, is sometimes recommended with great benefit in this way even 150 to 240 gr (10 to 16 gm) may be administered in a single day Rarely is it necessary or possible to continue such a large dosage for more than a few days. For children the dosage of salicylate may be halved and for infants one fifth to one tenth of the amount given to adults should suffice, but of course this medicine will rarely be needed at such an early age.

Intravenous salicylate therapy in large dosage has been tried out, controlled by testing the concentration of the drug in the blood (Coburn, 1944) but its early promise, like the saturation by oral salicylates a good many years ago, has not been confirmed. Thus the statements made in the previous editions of this book still hold, namely that the antipyretic effect of salicylates, if constantly given, may conceivably be harmful by masking some of the evidences of activity of the infection and so misleading one into a false sense of security and that if salicylates are used they should be employed only for symptoms of discomfort due to exudative reactions to the disease and occasionally

omitted for a few days at a time to determine the "true" course of the disease (temperature, leukocyte count, and signs and symptoms) However in the course of the trial of intravenous salicylate therapy a useful test for blood salicylate content was devised. It has been demonstrated, incidentally that as high a blood concentration of salicylate can be secured by oral administration as by intravenous. Finally a warning is due as to the toxic effects of salicylate poisoning including a tendency to bleed and even delirium—such toxicity is more readily produced by intravenous administration.

Vitamin C therapy Apparently midway between the effects of ACTH and salicylates is that of massive doses of vitamin C, the favorable effect of which has recently been described by Massell, et al., 1950 Acute rheumatic involvement has been controlled in a series of cases by the administration of 1 gm of vitamin C in orange or apple juice four times a day The exact mechanism by which this effect is produced is still obscure.

No place has been found for antihistaminic drug therapy in rheumatic fever despite the common supposition that this disease may be related to the allergies.

Serum treatment of the acute rheumatic infection, whether or not the infection involves the heart, has never evolved from the experimental stage. The use of specific" monovalent or polyvalent streptococcus vaccines has also been suggested and tried, but further study is needed before definite conclusions can be reached. A possible success of such therapy is to be ascribed rather to the reduction of streptococcus infections which may excite the rheumatic infection than to the primary control of the rheumatic infection itself

A much more important prophylactic measure recently introduced that bids fair to reduce the incidence of the "rheumatic infection in initial and especially in recurrent attacks has been, first, the administration of sulfonamide drugs in small dosage routinely throughout the winter and spring to susceptible children (e g. 1 0 to 1 3 gm, 15 to 20 gr sulfanilamide, divided into 2 or 3 doses, daily to a child of 8 years) to ward off, or in larger dosage to treat, the hemolytic streptococcus infections that so often precipitate active rheumatism and heart disease (Thomas, et al., 1939 1941 1942 Coburn, 1941 Hansen et al., 1942 and Kuttner and Reyersbach, 1943) and more *promising still of late, the use of penicillin, especially at the time* of exposure to a "streptococcus sore throat" or when such is just beginning (Mallner and Amsterdam, 1947 Goerner et al., 1947 Milzer et al., 1948 Massell, et al., 1948 Denny et al. 1950) A daily oral dose of 100 000 to 300,000 units of penicillin has been found apparently effective (Pitt Evans, 1950- Massell, personal communication, 1950) Similar preventive medicine may hopefully be practiced during acute infections or operative procedures (especially dental extractions) in the case of individuals with chronic rheumatic heart disease to ward off subacute bacterial endocarditis. We still await, however the final word as to the efficacy of these drugs in the prevention both of rheumatic fever and of subacute bacterial endocarditis.

It is to be noted that neither penicillin nor streptomycin nor the sulfonami have any favorable influence on the rheumatic process per se, in fact the t latter may cause harm by their toxic effect.

The *treatment of chorea* has been no more satisfactory than that of rheuma fever Absolute rest and quiet, with good nursing care, are more effective th any other measures. Neither arsenic (e g., Fowler's solution) nor the salic ates, nor other drugs or serum appear to have any specific action in co trolling chorea except for a promising recent experience with hormonal thera (adrenocorticotropic hormone) For very severe (convulsive) chorea m nesium sulfate intramuscularly intravenously or intraspinally (in 25 per c solution) has been reported to have a sedative effect. Phenobarbital (Lumina barbital (Veronal) or other mild sedatives, tincture of stramonium, a continuous baths have also been recommended. Febrile therapy by the i of foreign protein such as typhoid vaccine has also been used, but this, a matter of fact, may do harm by inciting an attack of rheumatic fever (Bla and Jones, 1935)

The *convalescent care* of patients suffering from subacute rheumatic infe tions, long continued and lasting for weeks, months, or even years, has be a problem attracting much attention in recent years. It is generally agreed th the active stage of the infection should be treated by rest in bed, but the comes a time when it is difficult or impossible to be sure whether or not t infection has completely subsided. In the case of restless children who fe well enough to run about and whose control is difficult at home much discr tion must be used, for such cases institutional care where the discipline good, or supervision by able nurses, may be essential during the active sta of the infection. When, with the patient at rest in bed and not taking salicylate the temperature no longer rises over 99 F by mouth, or 100 F by rectur the leukocyte count remains below 9 000, the sedimentation rate becom normal the pulse rate keeps under 100 symptoms and signs of infection ha disappeared, and the nutrition is improved, convalescence may be considere to have begun. The further length of time after that during which rest in be should be continued and the rapidity at which convalescence should b allowed to proceed to full normal activity should not be determined by an set rule (some have been suggested) but by the conditions in the individu case. After severe infection a minimum of several months of convalescenc should be prescribed before return to normal activity during this period foster home or preferably the child s own home should be utilized with train ing of the family to cope properly with the situation.

Removal of the patient to a *tropical climate* for example, Puerto Ric (Coburn 1931) or southern Florida (our own experience, Jones, White Roche, Perdue, and Ryan, 1931 to 1936 inclusive, reported in 1937) from the north during the colder seasons has been found generally to act favorabl in restoring health to children who show an active rheumatic state although beneficial as a rule, it cannot be regarded as specific and it is an expensiv

procedure often not justifiable. Permanent residence in the tropics is preferable if a "rheumatic" family can readily arrange it.

During convalescence massage and then the simple exercises of walking, lifting, and carrying will help to restore normal circulation and muscle function in the extremities. Special graded exercises are not necessary if common sense is used. Of great help in many cases has been recreational and even occupational therapy during convalescence and during the acute infectious stage membership in the "In-Bed Club for Children," developed by Edith Terry of the Massachusetts General Hospital, has greatly aided the morale of many hundreds of youngsters and their families.

Tonsillectomy is advisable in many patients with chronic rheumatic heart disease, provided their tonsils are infected or abnormally large and provided their hearts are in satisfactory condition to stand the operation, as they usually are. It is also to be recommended in many cases following active rheumatic infection *after* convalescence is well established. It has been advised and carried out even during the acute stage of the infection, apparently sometimes with immediate benefit, but certainly sometimes with exacerbation of trouble this procedure is not to be recommended in most cases during the active process. The prophylactic effect of *routine* tonsil removal in the case of rheumatic infection (rheumatic fever chorea, heart disease) has, however been disappointing; there has been only slight evidence that it protects against either initial or recurrent attacks. If the tonsils are, however infected or enlarged or if there are repeated attacks of tonsillitis, complete tonsillectomy should certainly be done in such cases it is undoubtedly beneficial in the long run. The adenoid tissue in the nasopharynx should be removed with the tonsils. If the operation is done in very young children it usually has to be repeated after some years because of the new growth of lymphoid tissue in the pharynx.

Roentgen irradiation of the heart has also been tried in the therapy of active rheumatic infection (acute endocarditis and myocarditis) but its value has not been confirmed.

Surgical treatment of chronic rheumatic heart disease is limited to but very few cases. Despite the failure of mitral valvulotomy over 20 years ago, renewed attempts are underway at present to apply surgical therapy to valve defects, but it is as yet too early to gauge the results or even to prophesy the various technics that will be applied, even plastic replacements have been suggested. One special condition due to rheumatic heart disease has, however already been dramatically helped by surgery and that is recurrent pulmonary edema secondary to tight mitral stenosis. Three methods have been used which will be described in more detail in Chapter 26. They consist of (1) production of an atrial septal defect to relieve the high pressure in the left atrium and lungs, (2) more practically and effectively to anastomose a right pulmonary vein to the vena azygos major and (3) probably best of all, the surgical separation at their commissures of the adherent cusps of the mitral valve.

For acute pericardial effusions paracentesis is necessary in rare cases only Chronic pericarditis of rheumatic origin is not the type requiring surgery in contrast to that due to tuberculosis.

Prevention. The prevention of rheumatic fever and thereby of rheumatic heart disease has become a practical reality It consists to date of several procedures (1) improvement of living conditions, (2) protection against hemolytic streptococcus infection by contact with an infected individual, (3) the prophylactic use of penicillin in the case of a susceptible person when there is such contact or when such infection begins in the individual concerned, and (4) avoidance, when possible, of residence in climatic areas (high and cold in particular) where hemolytic streptococcus infection and rheumatic fever are common.

Differential diagnosis. Rheumatic heart disease in active form has to be differentiated from any acute infection, especially if there happen to be heart murmurs. The differentiation is generally easy in older children and adults because of joint and heart signs and symptoms, but in very young children in whom the rheumatic infection is ill defined the problem may be a very difficult one, to be solved only by continued and careful observation. In young adults with chronic rheumatic heart disease it may sometimes be difficult to distinguish at first whether a new infection is a recurrent rheumatic attack or subacute bacterial (Streptococcus viridans) endocarditis. The fewer joint symptoms, longer course, wider temperature swings, greater anemia, and eventual appearance of characteristic signs of embolism, clubbed fingers, splenomegaly and positive blood culture gradually allow the differentiation of subacute bacterial endocarditis from acute rheumatism. The intradermal reaction to the toxic filtrate of the hemolytic streptococcus is generally positive in the rheumatic infection and generally negative in subacute bacterial endocarditis this is helpful but not conclusive It is important to note that the active rheumatic infection and subacute bacterial endocarditis may occur simultaneously in the same case (Kelson and White, 1945)

Septic, chronic, or rheumatoid arthritis offers as a rule, little difficulty in the differential diagnosis except when there happens to be a complication of heart disease or delayed A V conduction, or when both diseases are present in the same case then careful study is needed. Rare cases are, however insoluble there being no sharp boundary line, especially between rheumatoid arthritis and rheumatic fever

Chronic rheumatic heart disease must be differentiated from conditions like severe anemia which give rise to functional cardiac dilatation and murmurs. This is generally easily done by the discovery of the underlying cause, such as anemia, and by the history which shows that the heart symptoms or signs appeared for the first time after the onset of the underlying disease.

The rheumatic type of heart disease must be differentiated from other types, not always an easy procedure. The age, the history of rheumatic infection, family incidence the preponderant mitral valve involvement, and the absence of other causative factors like syphilis, thyrotoxicosis, hypertension, and cor-

onary disease usually distinguish primary rheumatic heart disease from other types. It is to be remembered, however that two or three different factors may simultaneously cause heart disease in a given case much care and good judgment must be exercised not only to determine these causes but also to decide their relative responsibility

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CHAPTER 15

ACUTE AND SUBACUTE BACTERIAL (INFECTIVE) ENDOCARDITIS

Penicillin and other new specific therapeutic agents have already greatly reduced the seriousness of the diseases discussed in the present chapter and we may hope that eventually the reduction or even complete control of hemolytic streptococcus and other infections and of rheumatic and congenital heart disease may render it obsolete. Much of what was printed in earlier editions of this book is now merely of historical interest.

A discussion of acute and subacute bacterial (infective) endocarditis (malignant endocarditis) follows naturally after the last two chapters, because bacterial endocarditis has been frequent in early adult life and has been in its subacute form an important complication of rheumatic and of congenital heart disease.

These two types of cardiac infection have been called acute bacterial endocarditis and subacute bacterial endocarditis respectively because of their clinical characteristics. This terminology is useful for general discussion and classification, but not so satisfactory as is the terminology based on the specific causative bacteria, the names of which should always be employed in preference to the general term, provided we know what the bacteria are. For example, Staphylococcus aureus or pneumococcus endocarditis is preferable to acute bacterial endocarditis as a diagnosis, and Streptococcus viridans or alpha hemolyticus endocarditis is a better term than subacute bacterial endocarditis. The word "infective" is sometimes employed instead of "bacterial," and in former days both of these groups of infection of the heart were classed together as "malignant" endocarditis, a designation with much justification because of the almost invariably fatal outcome in those days, but unsuitable because of the customary restriction of the word "malignant" to new growths and because of the high recovery rate nowadays.

In a large series of cases of acute and subacute bacterial endocarditis (199 cases with 138 autopsies) studied 25 years ago the responsible organisms were found as shown in Table 7, page 386.

Acute and subacute bacterial endocarditis are alike in that they are both serious diseases attended by invasion of the endocardium by virulent organisms almost wholly of the coccus family; there may be a similar invasion of the walls of the great arteries (bacterial endarteritis). The duration and virulence of the diseases are the only points in which they differ clinically. An arbitrary borderline of two months has been set between them. If the infection is a violent one lasting but a few days or weeks it has been called acute bacterial endocarditis; if it is slow in its course lasting over two or three months

Table 7

BACTERIA CAUSING INFECTIVE BACTERIAL ENDOCARDITIS

	Per Cent
Streptococcus	57
Pneumococcus	14
Staphylococcus aureus	13
Gonococcus	11
Influenza bacillus	4
Staphylococcus albus	1 (Thayer 1925)

it has been called subacute bacterial endocarditis. Generally the latter is caused by one organism, the Streptococcus viridans, while the former is caused by any one of a large number of organisms. Rarely a Streptococcus viridans infection is so rapid that it falls into the acute bacterial group, and rarely one of the other organisms is so much resisted that it falls into the subacute bacterial group, as happens infrequently in the case of the gonococcus or of the influenza bacillus.

A high mortality was once characteristic of these diseases, prior to the use of penicillin early in 1944, but now recoveries are the rule and preventive measures are also highly effective, especially in the case of the acute type. Mild infection with these organisms resulting in demonstrable valvular deformity after recovery may possibly account for some of the chronic valvular disease found in cases without a history of a rheumatic infection, but the extent to which this occurs is not actually known and must be regarded still as an open question. In the present state of our knowledge it is reasonable to assume that the majority of cases of chronic nonsyphilitic valvular disease are rheumatic in origin.

Finally there is a considerable number of cases of very fresh endocarditis of slight or moderate degree discovered only by the pathologist at postmortem examination of individuals dying of a great variety of diseases. Such terminal endocarditis is of academic and pathologic interest alone for it usually cannot be diagnosed clinically and has little or nothing to do with the death of the patient. We do not ordinarily designate under the term acute bacterial endocarditis this slight terminal endocarditis that has little or no clinical significance.

ACUTE BACTERIAL ENDOCARDITIS

Acute bacterial endocarditis or endarteritis consists of an acute nonrheumatic invasion of endocardium or arterial endothelium either uncomplicated or as a part of other acute illness It is attended by the symptoms and signs of severe infection and in days gone by ended often, in fact usually in death in the course of two months, but now recovery is the rule in the rare cases that still appear Cases in which it occurs number well under 1 per cent of all types of heart disease and of all types of endocarditis, if we exclude the terminal endocarditis that has no clinical significance.

Etiology *Cause* The bacterium responsible for this disease may be any one of several organisms, generally either the Streptococcus hemolyticus, the Staphylococcus aureus, the Bacillus coli communis, the pneumonococcus, the gonococcus, or the meningococcus These six infecting organisms had been found in acute bacterial endocarditis in Boston before the days of penicillin in the following relative frequency making up nearly 100 per cent of the total of cases the Streptococcus hemolyticus 43 6 per cent, the Staphylococcus aureus 22.8 per cent, the Bacillus coli communis 10.5 per cent, the pneumococcus 8.4 per cent, the gonococcus 4 2 per cent, and the meningococcus 4 2 per cent (Phipps, 1932, with additional data by Dexter personal communication, a total of 48 autopsied cases of acute bacterial endocarditis)

Other bacteria that have been reported as rare causes of acute bacterial endocarditis are the Staphylococcus albus, the typhoid bacillus, the enterococcus, the Micrococcus tetragenus, the Bacterium acidi lactici, the Streptococcus viridans, the parainfluenza bacillus (Russell and Fildes, 1928 Fox, 1935) the plague bacillus, Brucella melitensis (Malta or undulant fever bacterium) and the Micrococcus endocarditidis rugatus.

These organisms enter the circulation and attack the heart usually in the course of severe illness elsewhere in the body such as pneumonia, puerperal infection, gonorrheal rheumatism, abscesses, pyemia, tonsillitis, and meningitis. In one series of 400 fatal cases of pneumonia examined post mortem 22 instances of pneumococcus vegetative endocarditis were found (Menetrier 1919) and in another series of 337 fatal cases of pneumonia there were 14 cases of pneumococcus endocarditis (4 15 per cent) (Lord, 1932) In a series of 402 fatal cases of puerperal fever acute streptococcus endocarditis was found 8 times (Ruiz and Garcia, 1926) Happily all this is now essentially past history since there is at present specific therapy for almost all these primary infections.

There is another source of infection that is not yet under adequate control and that is septicemia (especially with a staphylococcus) resulting from the self-medication hypodermically by narcotic addicts (Hussey et al 1944 Luttgens, 1949) In such cases there is usually no pre-existing valvular disease.

Age Acute bacterial endocarditis may occur at any age from infancy to

old age, but it is most frequent in the fifth decade. It may rarely occur also in fetal life.

Sex Males are more subject to the disease than are females (73 per cent males to 27 per cent females in Phipps series, 1932)

Predisposing factors Although this acute cardiac infection may occur in hearts previously undamaged, it is more likely to attack those hearts already diseased, with rheumatic lesions or congenital defects or arteriosclerotic changes, where the soil is more suitable (60 per cent of Phipps series, 1932)

Pathology In acute bacterial endocarditis the valve cusps, and frequently also *the chordae tendineae and endocardium of atrium or ventricle* (more commonly the left) and sometimes even the intima of aorta or patent ductus arteriosus, are the site of the deposition of thrombi, called vegetations these vegetations are of varying size sometimes as large as peas or beans, and they consist of irregular masses of fibrin, leukocytes, and colonies of bacteria. Any valve may be markedly involved, but the pulmonary is only rarely affected. In acute bacterial endocarditis, though less strikingly than in rheumatic heart disease, the valves of the left side of the heart are more frequently involved than those of the right side. The aortic valve is about as frequently affected as is the mitral In a series of 23 cases of pneumococcus endocarditis, the left side of the heart was involved alone in 18 the right side alone in 3, and both sides in 2, while the mitral valve was affected in 13 the aortic valve in 12, both mitral and aortic valves in 5 and the tricuspid in 5 in one of which the pulmonary valve also was involved (Lord, 1932) In a series of 58 cases of gonococcus endocarditis the valve lesions were left-sided in 48, and the aortic valve was involved in 35 of these (Lion and Levy Bruhl, 1922)

Ulceration of the endocardium of valve or heart wall or of the wall of the aorta or other arteries is common in the more severe cases this is sometimes followed by perforation or aneurysms of cusps, rupture of chordae tendineae, abscesses of the valve rings, and even by small aneurysmal cavities in the aortic or other arterial wall (called mycotic aneurysms)

With recovery scarring undoubtedly takes place, but whether or not such recovery is responsible for a few of the cases of chronic aortic or mitral stenosis we have no certain knowledge.

Coincident myocardial or pericardial disease is uncommon. There may be *found pyemic abscesses in the heart muscle or infarction due to* coronary embolism arising from thrombi on the endocardium septic pericarditis is also possible in such cases but is rare.

Symptoms. The symptoms of acute bacterial endocarditis are simply those of any very severe infection with septicemia fever of septic type with wide swings as a rule, often with normal temperature in the morning and 103 104 (40 C) or 105 F in the evening, chills and sweating, prostration, and delirium. In addition, if the disease continues as long as a few weeks, there tend to be symptoms from embolism caused by pieces of the endocardial thrombi blocking arteries to viscera, extremities, or brain, and pain and other localizing symptoms, such as hemoptysis from pulmonary infarction or hemiplegia from

cerebral embolism. The involvement of the heart itself rarely causes symptoms.

Signs. The patient appears very sick with little to point to the source of trouble, except for embolic phenomena and the appearance of anemia and heart murmurs (or their increase) if the disease lasts long enough. Sometimes there are no definite signs, the fever being accounted for by other evidence of infection, while the heart condition is discovered only at postmortem examination. There is usually a high (polymorphonuclear) leukocytosis, of 20 000 to 30,000 or more, unless the infection has completely overwhelmed the resistance of the patient. A secondary anemia develops rapidly but does not become so severe as in the subacute variety of bacterial endocarditis because of the short duration of the disease There may be petechial hemorrhages into the skin and in rare cases even extensive purpura. There may be defective atrioventricular conduction shown by increase of the *P R* interval of the electrocardiogram beyond 0.2 second, but this is rare Arrhythmias are very uncommon. The most important method of study is that of blood culture. In the presence of this disease a positive blood culture is usually obtained, at the second or third attempt if not at the first; the cause of the infection is thus discovered.

Course and prognosis. Acute bacterial endocarditis formerly progressed in rapid strides to a fatal termination in the course of days or weeks. Death was usually the result of toxemia, but sometimes it came from embolism of brain, lung, or coronary circulation. Very infrequently was it due to heart failure. The beginning of effective specific therapy by penicillin, the sulfonamides, and other medication during the past decade has changed the picture completely so that now fatalities are uncommon and acute bacterial endocarditis is usually "cured" before it starts by the control of the underlying disease, whether pneumonia, meningitis, gonorrhea, or other *acute infection. Thus* the diagnosis of acute bacterial endocarditis has now become not only very difficult but also very rare. It can still be suspected by the careful physician who notes the onset of the heart murmurs of valvular involvement during the course of pneumonia or sepsis, and who observes the persistence of these murmurs and the development of cardiac enlargement on recovery

Complications. Embolism, secondary anemia, and heart failure have already been noted as important complications. Another occasional complication that may be serious or even fatal is the tendency to hemorrhages, such as may occur in any fulminating infection—purpura of skin, sclerae, and mucous membranes, and bleeding from nose, mouth, lungs, or gastrointestinal tract,

Treatment. In the second edition of this book, *fourteen* years ago, it was stated that "there is no specific treatment for the disease, except in the very rare case of meningococcus endocarditis, when the administration intravenously of active antimeningococcus serum may effect a cure," that "when the pneumococcus of type 1 or type 2 is responsible it would seem rational to inject antipneumococcus serum," that "in most cases of acute bacterial endocarditis all kinds of drugs, vaccines, and serums have been tried in vain," that

"transfusions also have failed," and that "the rare recovery except when antimeningococcus serum may help, is due apparently to the patient's own resistance, which is to be supported by every measure at one's command, chiefly by good nursing care, food, quiet, and avoidance of the administration of drugs except to relieve discomfort." A great advance was noted in the third edition seven years ago consisting of the use of the sulfonamide drugs (sulfanilimide, sulfapyridine, sulfathiazole, and sulfadiazine) which, by controlling the underlying infections from pneumococcus, gonococcus, streptococcus, and staphylococcus, prevented, in some cases at least, this serious, in fact previously fatal, complication of acute bacterial endocarditis, and now today we can happily record another perhaps final, spectacular advance since penicillin has appeared to help to wipe out this dread disease.

Differential diagnosis. The two chief difficulties in diagnosis come (1) from easy confusion with the subacute variety of bacterial endocarditis and (2) from confusion with severe infection of other nature, especially with persistence or recurrence of the original disease from which the endocarditis comes. In the former case the virulence of the acute variety of bacterial endocarditis, its shorter course, the recent history of other illness, and blood culture findings generally make differentiation clear In the latter case the differentiation may be impossible only the development of embolic phenomena, of severe anemia, or of murmurs pathognomonic of valvular involvement (usually an aortic diastolic murmur) may point eventually to acute bacterial endocarditis. It is impossible to distinguish the rare case of recovery with chronic valvular disease from one of rheumatic origin unless the pulmonary valve has been affected or the case has been observed during its development in the course of some serious infection like pneumonia.

SUBACUTE BACTERIAL ENDOCARDITIS (ALSO CALLED SUBACUTE INFECTIVE ENDOCARDITIS, CHRONIC ULCERATIVE ENDOCARDITIS, AND ENDOCARDITIS LENTA)

Subacute bacterial endocarditis as a clinical entity is much more common than is the acute variety of malignant endocarditis. It consists of the invasion of the heart—chiefly of the valves—by the Streptococcus viridans, rarely by the gonococcus or influenza bacillus until recently it resulted fatally after a lingering illness. Its frequency and seriousness make it of great importance. In New England 20 years ago it occurred in 1 to 2 per cent of all cardiac patients (White and Jones, 1928) in 7 to 8 per cent of persons with congenital cardiovascular defects (Abbott) and in about 5 per cent of cases of rheumatic heart disease. Because of its seriousness subacute bacterial endocarditis has a relatively high hospital incidence in comparison with rheumatic fever for example, in the years 1928 to 1931 there were 177 cases of subacute bacterial endocarditis admitted to the larger Boston hospitals in contrast to 772 cases of rheumatic fever (Morrison 1932) The advent of the sulfonamide derivatives ten years ago altered the situation, for the outlook

was no longer entirely hopeless as it had been a moderate number of cures were recorded, but the disease was still nearly 95 per cent fatal. It was early in 1944 that, with proof of the efficacy of penicillin (Loewe) the outlook suddenly brightened and now recovery is possible in at least 80 per cent of the cases. Despite this great change, in fact because of it, a clear recognition of the details of the disease has become all the more important since the earlier the diagnosis is made the sooner the curative treatment can be started and the less will be the added damage to the heart and the risk from the common and serious complications such as embolism.

Etiology *Cause* The organism responsible for subacute bacterial endocarditis is in 90 to 95 per cent of the cases the Streptococcus viridans (Schottmüller 1910) and in the other 5 to 10 per cent the gonococcus, influenza or parainfluenza bacillus, enterococcus, or Brucella abortus. The typhoid bacillus has also been reported to give rise to a long-drawn-out endocarditis. There may be a mixed infection as by gonococcus and streptococcus (Orgain and Poston, 1942 Olinger 1948) or there may be more than one strain of viridans streptococci in the same case (MacLean and Howell, 1947) All these other organisms, especially the gonococcus, can cause a short, virulent, acute bacterial endocarditis but the Streptococcus viridans rarely does so

Predisposing factors The chief predisposing factor is chronic heart disease, particularly old rheumatic valvular disease (in about 80 per cent of the cases) and congenital cardiovascular defects (in about 10 per cent of the cases) especially in those with either bicuspid aortic valves (9 of 32 cases of Abbott s series and 11 of 52 of Gelfman and Levine s series) or ventricular septal defects (13 of 50 cases and 13 of 31 cases respectively) or patency of the ductus arteriosus (21 of 92 cases and 4 of 14 cases) or coarctation of the aorta (7 of 70 cases and one of 10 cases) in contrast to atrial septal defects (2 of 68 cases and none of 45 cases respectively Abbott, and Gelfman and Levine, 1942) but a previously undamaged heart may infrequently also be the site of this disease. Rarely aortic valves damaged by syphilis may be involved in subacute bacterial endocarditis, but in such cases there may be a coincident rheumatic valve lesion.

Focal infection, as in diseased teeth, tonsils, and gums can be a predisposing factor (Weiss, 1934) dental extractions are more commonly followed by subacute bacterial endocarditis than are any other recognizable events. There is a clear reason for this as indicated by the findings of Okell and Elliott (1935) in 40 instances after multiple tooth extractions in the presence of extensive disease of the gums, positive blood cultures were obtained in 30 (75 per cent) in 60 instances after multiple tooth extractions in the presence of a moderate degree of gum disease there were positive blood cultures in 42 (70 per cent) and in 38 instances of the extraction of one or more teeth without detectable gum disease there were 12 positive blood cultures (34 per cent) The more often one inquires specifically about dental work or infection prior to the onset of subacute bacterial endocarditis the more often one finds it (up to about one third of the cases)

The mechanism of the endocardial involvement in subacute bacterial endocarditis has been variously considered. Direct blood stream infection of the endocardium damaged of old, with small thrombi or ulcerations as footholds for the streptococci that happen to be circulating in the blood, is probably the usual mode of involvement rather than the introduction of these organisms to the endocardium through blood vessels in the valves, but it is possible that both methods of infection exist. Although the Streptococcus viridans is an occasional invader of the blood stream even in normal persons, it causes no disease unless it enters in large numbers (as through foci of infection) or unless conditions favor its lodgment and growth, as in individuals with chronic heart disease.

Age The age at which subacute bacterial endocarditis occurs varies from early childhood to old age It is commonest between the ages of fifteen and thirty years. Of 250 cases in Kelson and White s series (1945) 6 were under ten years, 42 between ten and twenty 79 between twenty and thirty 53 between thirty and forty 39 between forty and fifty 21 between fifty and sixty and 10 over sixty The youngest cases on record are one and one half years old (Goetsch, 1938) two and one half (complicating congenital heart disease) and five years old, but the disease is very rare in young children. The oldest cases were eighty-two years of age, a man who had apparently sclerotic valvular changes as a background of his infection (Willius, 1940) and eighty seven years (Zeman, 1945) Streptococcus viridans bacteremia, without endocarditis, has been reported in two infants shortly after birth, the mothers being ill with subacute bacterial endocarditis themselves (Walser 1928) A collection from the literature has been made (Rost and Fischer 1928) of 64 cases under the age of fourteen years.

Sex. Subacute bacterial endocarditis occurs somewhat more often in males than in females In Kelson and White s series (1945) it was found in 161 males and 89 females, and in a series of 328 cases collected by Blumer from the literature the ratio was 60 per cent males to 40 per cent females (Blumer 1923)

Other factors Other factors such as race climate, and social and economic status are relatively unimportant compared to that of the presence of chronic heart disease mentioned above, except as they favor the predisposing cause, namely rheumatic involvement. However it is possible, though not yet proved that any illness, accident, or exposure to cold and wet, or to strain may help to precipitate the disease by favoring the bacterial invasion

Pathology The pathologic picture in subacute bacterial endocarditis is primarily that of involvement of the endocardium of valves by the deposition of irregular masses of fibrin, leukocytes, erythrocytes, and platelets, enclosing bacteria and products of bacterial degeneration, called vegetations (Figures 87 and 88 see opposite page) These vegetations are larger than the thrombi in rheumatic endocarditis, but they may not be so large as those of acute bacterial endocarditis. The chordae tendineae and left atrium and left ventricular endocardium are frequently involved by a spreading of the infection from the valve

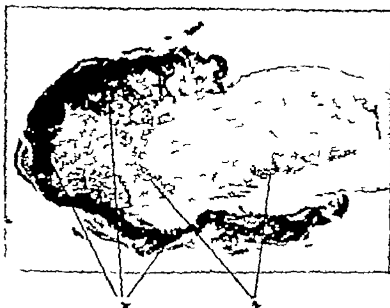


FIG. 37 Microphotograph showing low power magnification of the cross section of the end of cusp of the mitral valve infected by the Streptococcus viridans in subacute bacterial endocarditis. Note vegetation ( ) encircling the cusp end and consisting mostly of masses of bacteria, and fibrin (stained black) Also note inflammatory leukocytic reaction ( ) in the cusp itself.



FIG. 38 Photograph showing subacute bacterial (Infective) endocarditis with vegetation on mitral valve and endocardium of left atrium. (Kindness of Dr Ronald Grant, Guy' Hospital, London)

cusps or by contact with the cusps, that is, where the heart wall touches these vegetations on the cusp during the heart cycle. The intima of the aorta may also be infected, either where aortic valve vegetations are in contact with it or elsewhere. An arteriovenous aneurysm may become infected by the Streptococcus viridans. Finally congenital defects, such as patent ductus arteriosus, coarctation of aorta, and especially interventricular septal defects and bicuspid aortic valves may be the site of invasion by the Streptococcus viridans.

There may result from this inflammation of the endocardium an extension of the process into underlying tissues with deep ulceration, or perforation, or aneurysm formation in the valve cusps, or local ulceration and aneurysm of the aorta (even with rupture) This type of aortic aneurysm, like that resulting from acute bacterial endocarditis, is called a *mycotic aneurysm*. In very rare cases the process may cause an aneurysm in, or a perforation through, the ventricular septum, or from left ventricle into right atrium, or even a rupture of atrial wall. Also rarely invasion of the upper ventricular septal region may damage the atrioventricular bundle (of His) to cause heart block. The vegetations sometimes grow very large or elongated, and if this occurs on the aortic valve the vegetations may partially block the mouths of the coronary arteries.

The valves of the left side of the heart are much more frequently involved than are those of the right side, and the mitral valve oftener than the aortic, though the great preponderance of mitral over aortic valve involvement seen in rheumatic heart disease does not hold here. Pulmonary valve involvement is rare in subacute bacterial endocarditis, in contrast to its involvement in acute bacterial endocarditis. In a series of 90 autopsied cases of subacute bacterial endocarditis in which there was a specification of the valves that were involved in the process, the mitral valve alone was affected in 25 the aortic valve alone in 18 both mitral and aortic in 38 mitral, aortic, and tricuspid in 2, all four valves in 1 pulmonary and aortic in 2, tricuspid and ventricular septal defect in 1 pulmonary and ductus arteriosus in 1 pulmonary aortic, and ductus arteriosus in 1 and only the mural endocardium in the remaining 1 (Morrison, 1932)

As already noted, in the majority of cases Streptococcus viridans endocarditis is superimposed on chronic rheumatic valvular disease. It is probable that in communities where rheumatic heart disease is infrequent the predisposing factor of congenital defects is as important as is that of rheumatic valvular disease, and in such communities one would expect to find the total incidence of subacute bacterial endocarditis considerably reduced in comparison with that in "rheumatic" areas. Out of 203 cases of subacute bacterial endocarditis analyzed in Boston, 134 had clearly and others probably a rheumatic background, 11 had congenital defects, 3 an underlying syphilitic process, and one a definite atherosclerotic basis (Morrison, 1932) Markedly stenosed valves are less frequently attacked by subacute bacterial endocarditis the less slightly deformed valves in chronic rheumatic heart disease are the ones found at autopsy to be more often the site of this fatal complication, and they are the ones which during life give rise to the murmurs of valvular regur

pitation (the systolic murmur of mitral origin at the apex and the diastolic murmur of aortic origin at the base)

Pericarditis in subacute bacterial endocarditis is rare, but myocardial lesions have been reported (Bracht and Wächter 1909 Saphir 1946) consisting of diffuse inflammatory changes and of areas of infiltration in the interstitial tissue of the myocardium. These areas, however are also found in other cardiac infections and include the Aschoff body which may or may not indicate the presence of a coincident rheumatic heart infection in some cases. Saphir has also described foreign body granulomas caused by calcific emboli arising from healed vegetations on the aortic valve in patients recently treated with penicillin or the sulfonamides.

After recovery from subacute bacterial endocarditis the extent of chronic valvular disease may be increased. Since, however most of the valvular deformity is usually the result of previous rheumatic infection, careful observation of the state of the heart before or at the onset of the subacute bacterial endocarditis is essential before it can be said that this disease caused or increased the valve deformity in a given case

Symptoms. The symptoms of subacute bacterial endocarditis are like those of any infection but are less severe than in acute bacterial endocarditis. Fever of varying grades occurs, sometimes almost none at all and sometimes with wide daily swings of septic type, as, for example, normal or subnormal temperature in the mornings and high fever (to 104 F or 40 C) in the evening. Fever may however be absent for days at a time and then recur at intervals. Chills and sweats are common. Anorexia, malaise, prostration, and loss of weight and strength are usual, although for days or even weeks at the onset there may be merely a feeling of fatigue with little fever When embolism begins, coming from thrombi in the heart, local pain and other symptoms appear, depending on the organ or the part of the body affected. Splenic, renal, and cerebral infarctions are common. With increasing anemia there may be hemorrhages into skin, and from nose, lungs, and stomach—in addition to the embolic phenomena. Finally if the disease is not brought under control the toxic state increases and weakness and mental confusion may become marked before death ensues, or myocardial failure may develop, with dyspnea or hepatic congestive pain or both, if the infection is exhausting, whether or not it is itself cured. However with successful penicillin therapy at a relatively early stage of the disease nowadays, alert medical attention can, in the majority of cases, stop the process before any important complications take place

Signs. The characteristic signs of the disease are fever a pallor due largely to secondary anemia and sometimes referred to as cafe au lait (Libman) petechial hemorrhages into the skin, mucous membranes, and conjunctivae, splenomegaly clubbing of the fingers, and evidence of valvular or congenital heart disease. Rarely are all these signs pronounced in any given case usually the diagnosis must rest on two or three only generally supported, however by a finding of the Streptococcus viridans by blood culture.

The superficial *petechial hemorrhages* may be found anywhere on the body

and should be searched for carefully: they may be limited to the conjunctivae, to the chest, or elsewhere. They are most commonly found on the forearms and hands; when located under the nails they are linear in shape and have been designated "splinter hemorrhages." They come and go, often in crops in a given area; each spot rarely lasts more than a few days, beginning as a small reddish or purplish dot under the skin, not disappearing on pressure but gradually fading away within a week. The spots vary in size, usually from that of a pin point to that of the head of a large pin. They may be produced in the forearm from the compression of the upper arm by a blood pressure cuff. Thus they are evidently the result of damage to vessel walls by a toxin which allows leakage of blood whenever pressure, trauma, or some other factor favors it. The petechiae are therefore related rather to a hemorrhagic tendency of which a common sign is nosebleed, than to embolism. Petechial hemorrhages, although very common in subacute bacterial endocarditis, are not pathognomonic of the disease; they are also found not uncommonly in acute rheumatism.

There is another sign of vascular origin often of value but not found in all cases of subacute bacterial endocarditis: "tender fingers and toes." This is due most commonly to embolism of, or hemorrhage from, a small vessel in a finger tip or in a toe and consists of a deep, painful, purplish, slightly swollen, indurated area the size of a pea, or smaller, in the pulp of the end of the finger. This lesion comes suddenly and disappears gradually in the course of a few days. It may be isolated, or there may be several such lesions at the same time or in succession. Either fingers or toes may present this sign, but more commonly the fingers are affected.

The so-called Osler's node (Osler, 1909), as described first by Mullen of Hamilton and later by Osler himself, is a much rarer phenomenon. It consists of a raised red nodule (never hemorrhagic) in the skin of finger or toe and not beneath it, ½ to 1½ cm in diameter, with a whitish point in the center, and lasting a day or two.

Still another sign and much the most important of those found in the fingers or toes of patients with subacute bacterial endocarditis is *clubbing*. This condition, also found in congenital heart disease and certain pulmonary diseases, is shown in Figure 63, page 298. In subacute bacterial endocarditis it is very variable in occurrence and degree. Clubbing is present in some measure in three quarters of all the cases, but is well marked in only one half or somewhat less, being most evident in the cases with enlarged spleens. It does not appear at the onset of the disease, but only when it is well advanced, after the first few weeks. Why it should occur in this disease has not been discovered, but it is likely that local disturbance of the circulation (instead of general anoxemia with cyanosis, as in congenital heart disease) causes capillary dilatation and increased soft tissue growth. Instead of cyanosis there is usually increased redness of the bulbous finger tips. When present, clubbing is an important sign and should always be heeded, but care must be taken not to confuse it with congenital or occupational abnormality of shape of the fingers. Although the

toes may be clubbed as well as the fingers, their clubbing is generally less obvious. Clubbing recedes with recovery and disappears completely

Splenomegaly is common in subacute bacterial endocarditis and its presence is a very helpful sign. However in about a third of the cases the spleen cannot be felt on physical examination. Its enlargement when evident is usually not great, a firm nontender edge being felt just below the left costal border On rare occasions it may become large enough to extend almost to the umbilicus. Like clubbing of the fingers, splenomegaly usually clears up with recovery

The presence of evidence of *chronic valvular disease* or of *congenital defects* is usual and is somewhat corroborative. One finds commonly an apical systolic murmur of mitral regurgitation, occasionally the early diastolic murmur of aortic regurgitation, and less commonly the murmurs of mitral stenosis, aortic stenosis, or congenital defects. Sometimes an important murmur develops in the heart under observation, indicating the onset or the increase of valvular deformity during this infection. There is usually slight cardiac enlargement. The heart may however appear normal on physical examination during most, and rarely during all, of the illness one may be misled thereby In such cases there may be endocarditis of a congenitally bicuspid aortic valve without enough actual valvular deformity to produce significant murmurs.

Arrhythmia due to atrial fibrillation complicating subacute bacterial endocarditis was formerly thought to be extremely rare in recent years it has been found that their coexistence occasionally though still uncommonly takes place, for example, McDonald (1946) has reported 36 cases of atrial fibrillation (12.6 per cent) among 286 patients with subacute bacterial endocarditis. Of these 36 cases 24 were carefully analyzed, 3 showed paroxysmal arrhythmia and 21 permanent. Of the 21 5 had the infection first, 6 had the arrhythmia first, and 10 had both when first seen. Premature beats are occasionally found but are of little importance. The rare occurrence of delayed atrioventricular conduction (heart block) suggests extensive involvement of the interventricular septum. Pericarditis is extremely rare in subacute bacterial endocarditis.

Blood pressure, roentgenologic, and electrocardiographic studies show little or nothing abnormal except for evidence of underlying valvular disease, congenital defect, or heart block which may or may not be due to the subacute bacterial endocarditis.

Blood studies are of much importance. *Secondary anemia* is common if the disease lasts six weeks or more, with red cell count between 3 and 3½ millions and hemoglobin at about 60 per cent somewhat lower figures of 2 to 3 millions of red cells and 40 to 50 per cent hemoglobin are also found, but less frequently In rare cases the red count may drop to one million or less with hemoglobin of about 30 per cent. A polymorphonuclear leukocytosis of slight to moderate degree (12,000 to 16,000) is common when there are complications such as embolism to spleen or elsewhere Infrequently it is higher but more commonly it is lower often being recorded at a normal figure. The blood smear shows achromia of red cells but only rarely polychromatophilia or change in size or shape of the cells. The platelets are normal. In a certain

small percentage of cases, perhaps 10 or 15 per cent, there are found in the blood smear occasional large endothelial phagocytic cells which are also found sometimes in other diseases their presence is somewhat helpful in corroborating the diagnosis. The sedimentation rate is usually accelerated.

Blood cultures carefully taken, and repeated once or twice if necessary should be positive for the Streptococcus viridans in about 90 per cent of the cases. A suitable culture medium is hormone broth with hydrogen ion concentration of *pH* 7 6 It is of interest to prepare "pour plates" in order to get some idea of the quantity of organisms by the number of colonies per plate, which may vary from one to many Blood is collected in citrate flasks (½ cc of 4 per cent sodium citrate in a 50 cc Pyrex flask) from which 2 cc and two 1 cc samples are pipetted into tubes of melted nutrient agar which is cooled to 45 C, after the tubes are rolled a few times the mixtures are poured into Petri dishes and the colonies are read after two and four days (kindness of Dr Louis Dienes) Cultures of venous blood usually suffice but on rare occasions cultures of bone marrow are positive when blood cultures are negative. Arterial blood cultures are least satisfactory (Salazar-Mallen, et al., 1947)

Titration of immune bodies in the blood in patients with subacute bacterial endocarditis has shown a high degree of such bodies, much greater as a rule, than in the blood of the normal control. This test may perhaps prove helpful in establishing the diagnosis.

The Wassermann reaction has sometimes been found positive in subacute bacterial endocarditis in the absence of syphilis this possibility should be remembered.

The urine is not remarkable except for the frequent and important finding of numerous red blood corpuscles in the sediment. There usually is not enough blood to appear macroscopically This finding in the sediment has been ascribed to renal infarction by multiple small emboli. At postmortem examination glomerular lesions are frequently found (Baehr 1912) However it is probable that much of the blood in the urine is the result of minute hemorrhages, comparable to those in the skin (petechiae) Albuminuria is commonly present if there is much fever or bleeding.

Course and prognosis. The gradual, insidious onset of this disease often prevents any exact determination of the time of its beginning. There may be *a feeling of increasing fatigue and loss of appetite, and sometimes* there are vague joint and muscle pains the victim may appear pale, listless, and "run down" for a few weeks before fever or other symptoms force him to bed or to ask for medical advice. Months sometimes elapse with no definite idea of what is wrong. Usually however in the early weeks of the illness the temperature reaction anemia, enlarged spleen, or clubbing of the fingers, and heart signs and blood culture show the presence of this serious illness. Prior to 1944 the symptoms and signs would steadily increase, with development of embolic phenomena and death, often the result of complications, commonly ensued a few months to a year or more after the onset of the disease, the average duration of the illness being about six months.

Recovery prior to 1939 occurred in less than 1 per cent of all cases of subacute bacterial endocarditis rose to 5 or 6 per cent when the sulfonamides were introduced in maximal and very disagreeable dosage, and five years later in 1944 abruptly increased to a little over 50 per cent with the advent of moderate but still inadequate amounts of penicillin. Slowly in the five years that have elapsed since then, when penicillin became available in larger and larger amounts and with increasing realization of the need of massive doses early in the disease and with the help of allies such as streptomycin, at least 80 per cent of the patients have become curable It is likely that the ultimate figure will approach 90 but it is also probable that there will always be fatalities due to four causes (1) heart failure resulting from the extent of the heart disease itself plus the added strain of the infection and its treatment, (2) embolism to brain or elsewhere, and (3) intercurrent acute rheumatism, these three causes operating even in cured" patients, and, finally (4) resistance in a few cases to all specific therapy

It is to be remembered that a finding of the Streptococcus viridans in the blood by culture does not alone establish the diagnosis of subacute bacterial endocarditis, even if chronic valvular disease (or a congenital cardiovascular defect) or fever is also present, the presence of all three of these findings is, however almost conclusive in a given case Positive blood cultures have been found without fresh endocarditis, indicating that there is an illness of other nature present and not "malignant" endocarditis. A preponderant group of signs should be present to establish the diagnosis of subacute bacterial endocarditis. The clinical course is the most important clue. For full reliance on blood cultures several (at least 3 or 4) should be found positive.

There has been a very interesting small group of cases of subacute bacterial endocarditis, mostly of historic interest now that became bacteria-free but nevertheless went on for the most part to a fatal termination, from uremia or heart failure: they were characterized by the subsidence of fever negative blood cultures, anemia, brownish color of face, and particularly severe glomerulonephritis (Libman, 1913)

Finally advanced subacute bacterial endocarditis may be wholly or in large part symptomless prior to the occurrence of serious embolism, which in the case of a woman 31 years old led rapidly to death from coronary occlusion (West, 1931)

Complications. The chief complications of this disease are due to infarction of various organs from emboli that arise from the intracardiac (chiefly valvular) thrombosis. If these emboli are large and affect vital tissue a speedy death may follow The most important infarctions are those of the heart itself by coronary embolism of brain, and of kidneys. Cardiac infarction is very rare hemiplegia, or paralysis of lesser extent, is not uncommon after cerebral embolism, and hematuria may result from renal infarction or simply from leaking blood vessels. Hemorrhage of any serious moment is not often seen in this disease rarely it may complicate cerebral embolism and result fatally The renal damage may infrequently lead to uremia and death in a case of subacute

bacterial endocarditis. A large embolus may obstruct an important artery to an extremity like the femoral popliteal, tibial, brachial, or digital artery but rarely causes gangrene with need of amputation. The spleen is one of the most common sites of infarction thus explains the very frequent severe pain in the region of the spleen in patients with subacute bacterial endocarditis. Mesenteric infarction may occur and it has been suggested that some pulmonary signs may be due to embolism of bronchial arteries. Pulmonary infarction is not common inasmuch as the endocardial vegetations are generally or preponderantly on the left side of the heart, but with thrombi in the right heart chambers this, too, can occur A long course of febrile illness in a patient with congenital heart disease affecting the right heart chambers complicated by pulmonary infarcts strongly suggests subacute bacterial endocarditis In such cases blood cultures may fail to show the Streptococcus viridans until late in the disease, and clubbing of the fingers and splenomegaly may be wanting (Blumgart, 1933)

Heart failure of congestive type is sometimes, but not often, the cause of death it is frequently present in slight or moderate degree, brought on by the strain of infection and anemia in a heart already damaged rarely is there enough additional damage to the heart from this infection to cause failure directly Angina pectoris may rarely occur due to blocking of the mouths of the coronary arteries by the vegetations on the aortic valve, or to the added effects of aortic regurgitation and anemia. Atrial fibrillation occurs infrequently and heart block appears in rare cases.

Active rheumatism in the form of rheumatic fever or even of pancarditis may complicate subacute bacterial endocarditis, apparently excited by it in some cases and pre-existing in others It was thought to be a complication in at least 17 and perhaps 4 more of Kelson and White's series of 250 cases (1945)

The secondary anemia itself if not well controlled by transfusion, may become a grave complication, favoring a fatal outcome. In his weakened condition the patient may fall a victim to a complicating infection, like pneumonia.

Finally it is of some interest to note that pregnancy childbirth, and the puerperium may progress without any material difficulty despite subacute bacterial endocarditis (Mengert, 1935) although there may be Streptococcus viridans bacteremia in the infant (Walser 1928)

Treatment. In the first three editions of this book many different medicines and other empiric therapeutic measures were discussed but the only treatment that gave any promise at all was that with the sulfonamides, especially sulfadiazine which was the least toxic while effecting rare cures. When the sulfonamides were forced beyond the point of endurable toxic results there was a slightly higher percentage of recoveries. Doses of 2 gm of a sulfonamide followed in two hours by another 2 gm initially and then 1 gm every four hours until the blood level reached close to 10 mg per 100 cc, followed by adjustment of the dose to maintain that level, in the course of a fortnight or two resulted

in a few cures. Such supplementary therapy may still be of value when penicillin and streptomycin are alone or in combination ineffective. Heparin and Dicumarol were added to this sulfonamide therapy in the early days with the thought that they might prevent the deposition of new thrombi on the endocardium while those already present were being sterilized, but practical experience during recent years has indicated that such addition to the treatment has not resulted in any gain and instead has been troublesome, expensive, and even on occasion harmful.

It is of historic interest merely to insert herewith, without further comment except to note their failure, the imposing list of drugs and other therapy tried years ago in the vain effort to cure this dread disease: arsenic in various forms, mercury, gentian violet, salicylates, antiseptics of all kinds, vaccines, serums, transfusions including those from "immunized" donors, production of sterile abscesses, splenectomy, electrotherapy, diathermy, and hyperthermia. A few of these measures have had on occasion a somewhat helpful, though not curative, effect; transfusions have so acted when there has been a severe anemia, and both splenectomy and hyperthermia have had their advocates.

Happily today one can be brief and explicit about therapy that is effective in the great majority of cases, as the result of the discovery reported by Fleming in 1929 that Penicillium notatum, a common mold, contained a potent antibacterial substance, of its purification and application by Florey and his colleagues in 1940, and of its curative effect in subacute bacterial endocarditis by Loewe in 1944. After the diagnosis has been established as early in the disease as possible, or if not proved, at least considered probable after careful study, penicillin should be administered at once in adequate dosage and continued as a rule for six weeks, with a range of four to eight, or as much longer as may be deemed necessary in any particular case. A dose of 500 000 to 1,000,000 units a day should be given parenterally; if for any reason oral medication is given the daily dose must be 5 to 10 times greater to produce the same beneficial effect. If after a week or ten days there is no obvious effect of the 500 000 to 1 000 000 unit dose on fever, clinical course, or blood culture, the daily amount should be multiplied five times. Even as much as 20,000,000 units a day for weeks has been necessary to effect a cure in rare cases.

Common mistakes, quite natural in the early days of such therapy because of the limited supply of the penicillin, were to give too little at the start and to increase the size of the dose too slowly and too cautiously. It is far wiser to give a larger amount than may be necessary at the beginning rather than to allow the infection to continue too long with the hazard of serious complications. It is, however, best of all routinely to adopt the procedure of in vitro testing of the sensitivity to penicillin of the causative organism, whether Streptococcus viridans or not, since there has been shown to be a very definite relationship between this sensitivity and the curative dosage (Hunter, 1946; Clark, et al., 1948). The great majority of the strains of the Streptococcus viridans are inhibited by 0.1 unit of penicillin per cubic centimeter of culture

medium and so do not need maximal dosage but a few require 0.2 to 0.5 unit and a very few up to 1 unit or more It has been helpfully advised that for the first, that is the more sensitive group, a daily dose of 500 000 units be given, for the second, that is, the intermediate group, a dose of 1 to 2 million units, and for the third, the most resistant group a dose of 5 to 20 million units a day If these maximal doses are still ineffective, adjuvant treatment with caronamide or streptomycin is in order (see below)

Various methods of administration of the penicillin have been introduced and they all have had their advocates as may be found on consulting the Bibliography of this chapter Intramuscular injections in sterile saline or aqueous solution every two to four hours (usually three) day and night were in use most frequently and proved to be quite practical and effective. Constant intramuscular and intravenous drips were also curative earlier and had the advantage of producing a more constant blood level but the disadvantage of inconvenience. Penicillin in oil and beeswax proved helpful in establishing a fairly uniform absorption and blood concentration although without high levels (Hewitt, 1947 Hoffman, et al. 1947) this procedure was especially convenient because it reduced the number of injections needed intramuscularly to two in twenty-four hours and was recommended in particular for prophylaxis as in the case of dental extractions. Recently there has come into more or less routine use a preparation of penicillin with procaine (which has a beneficial twofold effect of rendering the injection painless and slow in absorption) which can be very conveniently and effectively injected intramuscularly in the dosage of 300,000 or 600 000 units every six hours, giving satisfactory total daily doses of 1 200,000 or 2,400 000 units respectively

Another important means of maintaining a more or less uniform and especially a higher (threefold or more) concentration of penicillin in the blood, particularly useful in obstinate cases not responding well to lower concentrations, is by adding caronamide or benemid which blocks the ordinarily rapid excretion of penicillin through the renal tubules (Beyer 1947 Boger et al., 1947 1949 and 1950 Loewe et al. 1947 Meads, et al. 1948 Burnell and Kirby 1951) Four grams of caronamide are given orally every three to four hours or ½ gm of benemid every six hours for days to weeks in order to produce a blood serum concentration of approximately 30 mg per 100 cc which is necessary in order to maintain a threefold or more increase of penicillin level. The drug must be used with some caution, however in patients who have any suspicion of reduced kidney function beforehand and probably not at all when serious kidney disease is present. Also toxic symptoms, such as nausea and vomiting, may be induced in some cases. However the use of caronamide and benemid has resulted in cures by penicillin in cases not responding well without it.

Finally in cases, fortunately very few in number in which penicillin is ineffective it may be necessary to resort to streptomycin alone or in addition or even to add sulfadiazine This applies to organisms, particularly gram-negative bacilli and certain gram-positive cocci which are very insensitive to

penicillin. In such cases after the in vitro and brief in vivo testing with penicillin and in vitro testing with streptomycin, the latter should be injected intramuscularly in the dosage of 0.5 to 1.0 gm (preferably the larger dose) every six hours for days to weeks, depending on the clinical progress and toxic symptoms. This gives a blood concentration of streptomycin of some 10 to 20 units (or micrograms) per 100 cc, which is, as a rule far greater than the in vitro sensitivity of the organism causing the disease There are two difficulties which render streptomycin much less satisfactory to deal with than penicillin (1) the toxic effects which include especially vertigo, which may be permanent, secondary to labyrinthitis, fever dermatitis, and pruritis, and (2) increasing resistance of the organism to the drug. Despite these disadvantages there are well-established cures of subacute bacterial endocarditis by streptomycin. Much more rarely and more or less as a last resort, sulfadiazine may be added to penicillin or streptomycin or both in the oral dosage of 4 gm initially or 2 gm repeated in two hours followed by 1 gm every four hours until the blood level reaches 10 mg per 100 cc, with continuation at that level and finally other antibiotics besides penicillin are worthy of trial in the case of unusual and rare infectious agents not amenable to penicillin.

Mention should be made, of course, of the importance of the best nursing care in the treatment of this disease, of patient but optimistic attitude of both doctor and victim during the tedious weeks of therapy and of the early recognition and treatment of complications, such as congestive heart failure by the use of digitalis, low sodium intake and diuretics. In very rare cases, cure of infected peripheral blood vessels, as in instances of mycotic and arteriovenous aneurysms, has been effected by surgical excision.

Differential diagnosis. The four conditions from which it may be difficult to differentiate subacute bacterial endocarditis are (1) active rheumatic heart disease, (2) acute bacterial endocarditis, (3) infections of other nature with or without chronic valvular disease, and (4) blood diseases or severe anemia secondary to some other infection like malaria. The duration and average severity of subacute bacterial endocarditis, the relative infrequency and unimportance of joint pains or swelling, the clubbing of the fingers when present, the slight but usually not great enlargement of the spleen the moderate grade of secondary anemia, the finding of the Streptococcus viridans in the blood stream, and particularly the frequency of embolism in an infection not very virulent in nature distinguish this disease with little difficulty from others. It is, however important to remember that the various conditions cited above may coexist in the same case.

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CHAPTER 16

CARDIOVASCULAR SYPHILIS

Introduction. This is another chapter which we may justifiably hope and expect to become obsolete during the next generation, since already great progress in the reduction of cardiovascular syphilis has been actually demonstrated to the author and his contemporaries during the past generation by means of the prevention of syphilis itself in the first place, its earlier recognition and more adequate initial treatment in the second place, and its better therapy even in its later or tertiary phase in the third place.

In every chapter that has preceded the present one a considerable revision has been necessary as the result of the rapid strides of medical progress in the past seven years since the last edition of this book. Even more dramatically has progress been made in the subject of the present chapter in the way of preventive medicine. And yet, despite this advance syphilis continues to be, after rheumatism, the second most common and important cause of infectious cardiovascular disease. By the time the diagnosis of cardiovascular syphilis is made it is in most cases a very serious condition. Fortunately however it is a preventable disease, and already in many parts of the world it is on the wane and no longer common. In New England two decades ago it was found to make up 4 per cent of a large series of cases of cardiovascular disease (White and Jones, 1928) being more frequent in general hospital practice than in private practice; now however it makes up less than a quarter of that figure (that is, less than 1 per cent) Among the Negroes in the southern part of the United States, on the other hand, it is still a common though decreasing cause of cardiovascular disability and death, being a prime factor in about 20 per cent of cardiac patients, even there it is less frequent than the factor of hypertension. In a series of 414 Negroes in Texas with cardiovascular disease over twenty years ago syphilis was the chief factor in 32 per cent and hypertension in 50 per cent (Stone and Vanzant, 1927) there too however the recent public health campaign gives promise of a reduction in cardiovascular syphilis, such as has occurred elsewhere.

It is a very interesting fact, as yet unexplained, that syphilis damages the

aorta more than other arteries or the myocardium Cardiovascular syphilis consists primarily therefore, of aortitis with or without secondary effects on the heart, infrequently it means myocardial disease or involvement of great vessels other than the aorta, such as the femoral, carotid, and pulmonary arteries.

In a series of 50 000 consecutive autopsies in Minnesota over a period of thirty-seven years beginning in 1910, syphilitic heart disease, not including uncomplicated aortitis, dropped in incidence from a maximum of 2.04 per cent at the beginning to 0.23 per cent at the end in individuals 40 years of age or older (Clawson, 1950) the general incidence of syphilitic cardiac deaths (0.83 per cent) in this autopsy material is now less than that of deaths from calcific aortic valvular disease (1 3 per cent) Syphilitic aortic insufficiency ranked first in the manner of death in Clawson s series of cases of syphilitic heart disease (58.5 per cent) Deaths due to rupture of a syphilitic aneurysm were second with 21 per cent and those due to narrowing of the coronary orifices third with 18 9 per cent. There were relatively few cases of gumma of the myocardium.

In a series of 9,807 necropsies in Italy the incidence of heart disease due to syphilis was found to be 2 per cent (Venzoni 1939) In a Cincinnati hospital with a large proportion of Negro inmates, however the incidence of syphilitic aortitis in autopsies from 1926 to 1937 inclusive was reported to be much higher (at least 9 1 per cent) (Gelperin, 1940) while in the Philadelphia General Hospital the percentage dropped from 9 2 in the years 1927 to 1930 to 5 6 in 1935 to 1937 (there was a majority of Negro cases) (Welty 1939)

Etiology *Cause* The organism responsible for cardiovascular syphilis, the Treponema pallidum was discovered in a diseased aorta in 1906 (Reuter) but long before the discovery of the actual causative agent in syphilis the connection between that disease and aortitis was known, and for several centuries the production of aneurysms by syphilis was suspected (Paré, 1575 Lancisi 1724 and Morgagni, 1761) Gummata, long known to be of syphilitic origin, were early found in the heart itself

Although it is probable that the spirochete of syphilis invades the heart and aorta early in the disease at the same time that it invades other organs, actual disease of aorta and of heart due to syphilis is as a rule first demonstrable either by symptoms or by signs only a good many years after the primary lesion (chancre) Twenty years elapse on the average between the onset of the infection and its evident involvement of the cardiovascular apparatus, but there are wide variations, the intervals ranging from a few weeks to 30 or 40 years. Except in rare cases, clear evidence is wanting that there is any important involvement of the heart or aorta during the primary or secondary stage (that is, during the first few weeks or months) of the syphilitic infection most reports to the contrary are unsatisfactory Years ago, because of the lateness of this evidence of infection, aortitis and aneurysms were classed along with tabes dorsalis and general paresis as fourth stage or parasyphilitic lesions,

that is, the end result of the infection that had become inactive, while gummata, when they were found, were considered manifestations of the tertiary stage, still active. Now we know that all these processes are but different evidences of the syphilitic infection appearing late but still active a few aneurysms are relatively inactive scarred lesions, but such unprogressive aneurysms are uncommon.

There is obviously some sort of affinity between the treponema and the aortic wall, just as there is between this organism and the central nervous system in certain individuals what it is we do not yet know Most cases of acquired syphilis do not, however develop cardiovascular disease at least 90 per cent never show clinical or pathologic evidence of such involvement.

Congenital syphilis as well as acquired syphilis may cause cardiovascular disease, but the congenital syphilitic type is not common. The simple presence of treponemata in the heart muscle of a syphilitic fetus or child (a common finding at postmortem examination) does not constitute syphilitic heart disease there must be appreciable tissue reaction or destruction in addition. This is well illustrated by a report of a study of 939 children with congenital syphilis (McCulloch, 1930) 498 of these children were over two years of age and only 5 showed any signs of cardiovascular disease and in them such heart disease was clearly of rheumatic nature, of the other 441 children, who were under two years of age, 32 died, but only 3 of these were found to have syphilitic heart disease, while none of the 409 survivors showed any signs whatsoever of cardiovascular syphilis.

Age Because of the possibility of cardiovascular involvement by syphilis in fetal life and of the possible acquisition of the infection relatively late in life the age at which cardiovascular syphilis may show itself clinically or at autopsy varies from birth to old age The usual age of clinical manifestation, however is in the late forties the large majority of cases come to notice between the ages of 40 and 55 years. In one series of 95 cases there was one patient less than 10 years old, there were four between the ages of 20 and 30 eleven between 30 and 40, twenty-five between 40 and 50, thirty-three between 50 and 60 twenty between 60 and 70, and one over 70 (White and Jones, 1928) Among Negroes the age at which cardiovascular syphilis becomes evident is younger nearer 40 than 50 frequently in the thirties, and even rarely in the twenties. In recent years two more cases with syphilitic thoracic aneurysms who were under the age of 30 years have been reported (Evans, 1941)

Sex The male sex has far more cardiovascular syphilis than has the female. In the series of 95 cases mentioned above, 78 were male and 17 were female, a ratio of almost 5 to 1 (White and Jones, 1928) In another series of 70 cases the ratio was 6 to 1 (Nichols, 1940) In Moore's series the ratio was about 2 to 1 (Moore, et al, 1932) and in a more recent series of 199 cases of syphilitic aortitis found among 9 807 necropsies (Venzoni, 1939) there were 164 men and 34 women (5 to 1) This is undoubtedly due largely

to the far greater male exposure to syphilis and to the factor of greater physical activity

Other factors Other known etiologic factors in cardiovascular syphilis are *race* and *social and economic status* These are very important, since the members of most of the less civilized races are far more subject to syphilis, once it is introduced among them, than are those of civilized races, where social customs and measures of prevention and early treatment afford at least a certain amount of protection. Even in a civilized community the percentage of cardiovascular syphilis is greater among the inhabitants of lower social and economic order In Moore s series it was about twice as common in Negro as in white patients (Moore, et al. 1932) A large percentage of the population of some half civilized peoples is found to be infected with syphilis what per centage of those develop cardiovascular disease due to this infection we do not know because of the lack of accurate statistics we might at first thought believe that cardiovascular syphilis would be very common in such peoples, but that is not always the case as found out in Arabia by Paul Harrison (personal communication, 1940) who encountered only very rare cases of aortic aneurysm or aortic regurgitation in an active medical service over many years in a country riddled with syphilis. It seems likely that a relative immunity so far as serious effects are concerned, can be acquired in countries where syphilis has long been almost universal and but little treated. In Uganda, however cardiovascular syphilis is said to be common, comprising over half of all heart disease among Africans (Williams, 1938)

The more laborious occupations are also almost certainly a cause for early appearance and rapid evolution of aortic changes due to syphilis, because of the greater physical strain produced thereby

The factor of early and satisfactory treatment of the original syphilitic infection is undoubtedly one of much importance as it concerns the later development of cardiovascular disease of syphilitic origin, in civilized communities at least. This is only now becoming evident since it is only in recent years that antisyphilitic therapy has been planned and administered in any satisfactory degree to the majority of patients. An example of this effect is the decrease in the incidence of cardiovascular syphilis, both relatively and absolutely seen at the Massachusetts General Hospital in recent years. In 1914 Cabot reported 12 per cent of a group of 600 cardiac cases as due primarily to syphilis, in 1928 White and Jones reported 5 per cent of a series of 880 cardiac cases as primarily or secondarily of this type in the same clinic, while in 1949 we have found only 1.5 per cent among 1 000 cardiac cases' another interesting comparison in this hospital is that of the incidence of the diagnosis of aneurysm of the aorta in the ten-year period of 1900 to 1909 inclusive (113 among 51 875 cases, or 0 2 per cent) with that in the ten-year period of 1925 to 1934 inclusive (only 61 among 75 184 cases, or 0 08 per cent, despite the improved roentgenologic facilities for diagnosis) In Baltimore in 1932 Moore and his associates stated that not one of 117 patients with

early syphilis who received three or more courses of arsphenamine, and treatment with mercury during periods between the courses, presented any evidence of cardiovascular involvement during the period of observation (up to nine years after the infection) while 24 of 285 patients followed during the same period of observation who had received less than this amount of treatment were observed to acquire syphilitic aortitis aneurysm or aortic regurgitation. Adequate treatment for early syphilis almost certainly protects the majority of patients so treated against subsequent cardiovascular syphilis. Various procedures are now in progress in the use of penicillin in the rapid treatment of early syphilis, for example 600 000 units of procaine penicillin daily for ten days (Kossmann personal communication, 1949)

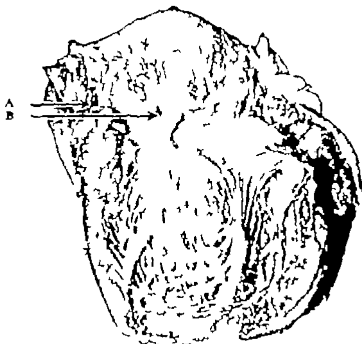


FIG. 89 Photograph showing syphilitic aortitis with marked narrowing of the mouth of the right coronary artery (*B*) the mouth of the left coronary artery (*A*) is slightly narrowed. Compare this with Figure 142. (Jores *Arterien*. Courtesy of Julius Springer Berlin.)

Pathology Cardiovascular disease due to syphilis is of three main types.

1 The first and commonest type is the result of *destruction of the media of arteries* The exact pathogenesis of this lesion is not known In the aorta it is thought to result from obliterative endarteritis of the vasa vasorum. It is most evident in the ascending portion of the aorta where the intima becomes pale and wrinkled due to the destruction of the media below it (Figure 89) The aortic wall is thus seriously weakened and loses its elasticity stretches and dilates. The intima is thickened becomes atheromatous, and may ulcerate

though ulceration is less common than in the case of primary atheroma. The spirochete of syphilis may sometimes be found in the diseased aorta.

Three important developments of this destructive syphilitic aortic process may occur; if no one of these is found, as sometimes happens, the condition then remains clinically unimportant. These three developments are (1) a stretching of the aortic wall to give rise either to a diffuse or spindle-shaped dilatation or aneurysm, or locally to a saccular aneurysm, (2) an involvement of the aortic valve to deform it and to cause aortic regurgitation, and (3) a narrowing of the mouths of important branches of the aorta by an extension of the process itself.

(a) *Aortic aneurysms* like syphilitic aortitis itself, most commonly involve the ascending portion of the aorta, less often the aortic arch, and least often the descending portion in thorax or in abdomen. They are only an occasional accompaniment of aortitis, being found in 10 per cent or fewer of the cases, but they are serious because of the pressure they often exert on surrounding structures and because of their tendency to rupture into pleural cavities, pericardial sac, bronchi or trachea, esophagus, mediastinum or even into other great vessels (pulmonary artery or superior vena cava). Aneurysms are still rarer accompaniments of other conditions, such as atherosclerosis, senile ectasia, trauma, or bacterial endarteritis. They are discussed further in Chapter 28 of this book.

(b) *Aortic valve disease with regurgitation* is a much more common accompaniment of syphilitic aortitis than is aneurysm, occurring in one quarter to one half of the cases diagnosed clinically though rarely early in the disease. It was found in 36.5 per cent of the 126 cases of syphilitic aortitis examined post mortem by Clawson and Bell (1927) and in 27 per cent of the series of cases of cardiovascular syphilis of Moore and his associates (1932) which in turn made up 10 per cent of a clinical series of 6 420 patients with various forms of late syphilis. It is due to a downward extension of the aortitis to involve primarily the commissures of the valve. The inflammatory process widens the commissures and, by separating the cusps, produces regurgitation (Figure 131 shown on page 686); this is the reverse of the rheumatic effect which unites the cusps at the commissures to cause stenosis rather than regurgitation. Extension of the syphilitic process may further damage the valve cusps themselves and cause their retraction or adhesion to the sinuses of Valsalva. A very interesting finding is a rather rare eventration of one of the aortic valve cusps, giving rise to a striking loud high-pitched musical aortic diastolic murmur with thrill (Bellet, et al., 1939; Nichols, 1940). A weakening of the aortic valve ring with stretching often comes with aortitis, and is probably more commonly the cause of aortic regurgitation than is valve deformity per se. Thus aortic regurgitation so frequently complicating syphilitic aortitis may result either from this stretching alone, or from damage to the valve, or from both factors. The other heart valves are not affected by the syphilitic process directly except as the anterior cusp of the mitral valve may be somewhat involved or deformed by spread of the inflammatory

reaction down over it from the aortic valve, or by retraction of the damaged aortic valve.

(c) *Narrowing of the mouths of the branches of the thoracic aorta* by the inflammatory syphilitic process is an important and not infrequent complication of the aortitis It may even advance to the stage of actual occlusion. *Coronary involvement of this nature* (Figure 89) *is particularly serious* and accounts in large part for the angina pectoris and especially for the sudden death so often occurring in patients with syphilitic aortitis. It was found in 25 per cent of the series of 126 autopsied cases of syphilitic aortitis of Clawson and Bell (1927) and in over half (105 out of 199) of the autopsied cases of Venzoni (1939) Although the coronary arteries beyond their mouths are usually not involved in the process, they may rarely be the seat of a syphilitic mesarteritis with narrowing and obstruction or even aneurysmal dilatation (Seydel, 1935) Other arteries—the innominate, carotid, subclavian, and intercostal—may also be more or less occluded at their mouths in syphilitic aortitis, especially if there be in addition aneurysmal dilatation, which compresses these arteries. Such obstruction may lead to decrease and delay of one or both of the carotid or radial pulses and rarely to their obliteration, with development of a collateral circulation to head or arms.

Other arteries besides the aorta and coronary arteries may be attacked by the syphilitic process with thickening of wall, thrombosis, and occlusion, or with stretching of the weakened wall and aneurysmal development. There may be aneurysms anywhere in the body In themselves aneurysms exert little or no strain on the heart, the strain comes if they perforate into veins (arteriovenous aneurysm) or if in the case of the aorta, the coronary arteries are obstructed or the aortic valve is deformed. Sclerosis of the pulmonary artery and its branches following syphilitic involvement of the bronchi and causing right ventricular failure and marked cyanosis ("black cardiacs") was described in 1901 (Ayerza, as quoted by Arrilaga in 1912—see bibliography of Chapter 20) but such a syphilitic sequela is excessively rare; the great majority of cases of cor pulmonale with right heart failure and marked cyanosis are not syphilitic (see Chapter 20)

2. The second type of syphilitic involvement after that of the arteries is a *diffuse inflammatory reaction in the myocardium* with the presence of spirochetes (Warthin, 1925 Magill, 1935) Some cases of sudden death have shown this syphilitic myocarditis, but it is an infrequent manifestation of cardiovascular syphilis. Rupture of a papillary muscle due to syphilitic myocarditis has been noted, but it is exceedingly rare.

3 The third type of cardiovascular syphilis is also rare and consists of the *invasion of the heart by gummata.* These localized reactions to the presence of spirochetes may be situated anywhere in the heart—atrial walls, ventricular walls, or septum. If they occur high in the interventricular septum they may involve the specialized conduction system of the heart—the atrioventricular bundle of His or its branches—and produce heart block of one type or another Gummata in the myocardium were found in only 3 of the 126

autopsied cases of Clawson and Bell's series (1927) Myxoid formations in the myocardium consisting of rounded translucid nodules have also been reported as a syphilitic lesion (Warthin, 1916)

Symptoms. Cardiovascular syphilis is often symptomless, not only in its early stages but sometimes even when it has become far advanced. It produces symptoms chiefly (1) by its involvement of the aortic valve which causes heart strain and eventual failure, or (2) by its narrowing of the coronary artery mouths or walls to cause angina pectoris and even very rarely acute myocardial infarction (Burch and Winsor 1942) or (3) by the pressure of aneurysmal dilatation on surrounding tissue to cause pain or to obstruct blood flow in other vessels, to block esophagus or air passages, or to occasion hoarseness by involvement of the recurrent laryngeal nerve, with paralysis. The aortitis itself is almost always symptomless but sometimes a more or less constant dull ache high under the sternum has been ascribed to it, even though there be no definite aneurysm.

The earliest and commonest symptoms associated with cardiovascular syphilis, which usually means aortitis, are, less commonly angina pectoris and, more commonly paroxysmal dyspnea with or without cardiac asthma or frank pulmonary edema. Either one or both may be present, with no other symptoms at all or all the symptoms of congestive failure—more or less constant dyspnea, weakness, and pulmonary and systemic edema—may supervene to replace the angina pectoris or to appear at the very onset of evident trouble. Sometimes pallor and loss of strength and weight also appear early in the disease.

Sudden death is quite common in cardiovascular syphilis with or without preceding symptoms It was reported as having occurred in 39 of the 199 cases (20 per cent) in the series of Venzoni (1939)

Signs. There may be no signs whatsoever of cardiovascular syphilis by any method of examination, and the condition may be discovered only at postmortem examination. Dilatation of the aorta, which occurs after the process has advanced considerably may also escape attention for some time, even after symptoms have appeared, unless careful roentgenologic study is made. Even when careful roentgenologic examination is carried out it is not possible to recognize early or slight syphilitic aortitis thereby for aortic dilatation and secondary calcification are after all rather late effects and actual dilatation of the first few centimeters of the aorta (a common site of syphilitic aortitis) may be present with no evidence by roentgen ray because the aortic shadow at its root is buried in that of the heart in all roentgenologic views and positions as carried out routinely However by the injection of a contrast medium, such as Diodrast, the root of the aorta can usually be delineated in doubtful cases.

Later on when the process has become extensive and has advanced to the stage of aneurysmal formation, of aortic regurgitation, or of coronary obstruction, ordinary methods of clinical examination may reveal it, but by that time the situation may be hopeless. Keen observation and careful study must

always be carried out when there is a suspicion of aortitis. Since symptoms and signs often appear only when the disease is advanced, however it will rarely be possible to pick up the early cases in spite of routine periodic examinations. Routine examinations nevertheless, especially of those individuals with a history of syphilitic infection, will sometimes reveal trouble that may be amenable to treatment before any symptoms have forced the patient to consult medical advice the value of these examinations should be universally realized.

With aortitis alone or with aortic aneurysm without aortic regurgitation or coronary obstruction, the heart remains normal in size without murmurs, but when aortic valve disease develops with increasing regurgitation the heart enlarges rapidly and may eventually increase to enormous size to produce the typical *cor bovinum*. With a considerable valve defect a loud aortic diastolic murmur develops, louder than is found as a rule in rheumatic aortic valve disease and often heard best at the right of the upper sternum a moderate to loud aortic systolic murmur also is usually heard there (due to the aortic dilatation) the heart sounds are masked, a functional mitral diastolic murmur (Austin Flint) is common, and the peripheral pulse becomes water-hammer in character along with the appearance of the so-called capillary pulse. Stenosis does not complicate the aortic regurgitation of syphilitic aortitis, although aortic stenosis, probably of rheumatic origin, has been encountered along with syphilitic aortitis (for example three such cases noted by Cabot, 1926) A curious loud high-pitched musical character may be imparted to the aortic diastolic murmur with development of a palpable thrill when, as already noted above, there is an eventration of one of the valve cusps (Bellet, et al. 1939 Nichols, 1940) It is to be remembered that the aortic regurgitation of syphilitic aortitis may begin gradually and at first may be but slight hence it is possible in some cases to find only a slight to moderate aortic diastolic murmur without a Corrigan pulse.

There are three signs that have sometimes been adduced as evidence of early syphilitic aortitis before the development of aortic regurgitation or of well-marked aortic dilatation, they are (1) an aortic systolic murmur (2) accentuation of or a tympanitic or metallic note to, the aortic second sound, and (3) increased retrosternal percussion dullness. These signs are all very unreliable, the first two being much more common in cases of aortic sclerosis with past or present hypertension, and the third being found only when there is marked aortic dilatation or a widening of or disease in, the mediastinum.

The *serum reaction* for syphilis (Wassermann, Kahn, Hinton) is generally positive, and strongly so, in cardiovascular syphilis sometimes, in approximately 15 per cent of the cases, it is negative the Hinton reaction is more sensitive than the Wassermann test. It must be remembered, however that syphilis with a positive Wassermann reaction may be present as an incidental infection complicating chronic valvular disease or angina pectoris which is not of syphilitic origin this fact accounts, I believe, for a gross overestimation of

syphilitic aortitis as a cause of angina pectoris in some parts of the world in days gone by

The essential evidence of syphilitic aortitis is most commonly presented by roentgen ray examination the bulging of the thoracic aorta (especially the ascending portion and the arch) without other adequate reason (for example, hypertension) affords the essential clue (Figure 146, page 770) The electrocardiogram remains normal until the heart enlarges as the result of aortic regurgitation, with the development then of the pattern of left ventricular hypertrophy and dilatation (see Chapter 9) or until the coronary circulation is interfered with, when one of the many patterns of coronary heart disease may appear

Course and prognosis. The onset of cardiovascular syphilis is very slow and insidious. When aortitis has becomes established years after the initial lesion and has come to light because of the symptoms or signs it has produced, the course is often difficult and the prognosis is often poor Sometimes, however treatment helps a good deal in relieving symptoms and in retarding the progress of the disease. Spontaneous cures or rather cessation of symptoms without further development of signs are also seen. Not infrequently in the course of a few months to several years after the discovery of the trouble death occurs suddenly with or without preceding angina pectoris, or it may result from congestive heart failure, some complicating infection or cerebral lesion, or rarely rupture of an aneurysm. Sometimes death comes quickly even in a few weeks sometimes it is postponed for ten to twenty or more years. The average duration of life from diagnosis to death used to be about three years it has been increasing steadily since more effective therapy has been carried out. One of the most important factors of all in controlling prognosis is the degree of physical activity of the patient the more strenuous the life in this respect, the shorter it will be, a relatively quiet existence undoubtedly prolonging life. This fact is a prime reason for the very serious prognosis of cardiovascular syphilis among the Negro laborers. Of 124 cases of syphilitic aortic regurgitation followed personally by Blackford, 57 died within one year of the discovery of the lesion, 27 more died during the next two years, 17 were known to be alive after three years, and 8 were still alive after five years (Blackford, personal communication, 1936) In all probability the factor of hard physical work is more important than that of race in this regard, although it is true that the relative neglect of treatment may enter also

The effect of "energetic" specific treatment even of this late syphilis of aorta and heart on prognosis has been, in the main, distinctly favorably as has been demonstrated by a number of authorities (Moore, et al., 1932 Padget and Moore, 1935 Buch, 1945 Webster and Reader 1948) A study of 116 patients (103 men and 63 women) with late syphilitic cardiovascular lesions showed the following relative survival periods for "well-treated," "moderately treated, and poorly treated" cases 71 months, 57 months, and 16 months respectively (Buch, 1945) Webster and Reader studied the microscopic

sections of the aortas of 45 patients with gross evidence of syphilitic aortitis at postmortem examination with relation to the effect of treatment. The patients were divided into untreated, inadequately treated, and adequately treated groups, the criterion of adequate treatment being a minimum of at least 20 arsenical and 20 bismuth injections only three of 19 patients adequately treated showed any activity of the process while all 9 untreated cases showed active cellular infiltration of the aorta.

Sudden death is occasionally the result of an undiagnosed syphilitic involvement of aorta or heart, without previous symptoms or signs. The medical examiner or coroner establishes the cause of death. If such cases were added to those in whom the diagnosis has been made before death, the statistics of the total number of cases of cardiovascular syphilis in the community would be slightly increased, but probably by not more than a very few per cent at most, depending of course on the thoroughness of medical examination and care and of postmortem examinations in that particular community

The prognosis may be made worse in rare cases by too vigorous therapy Heart failure and even death have followed directly in a few cases from overzealous efforts to cure

Complications. The important complications of cardiovascular syphilis have already been referred to under the heading of pathology—aneurysms, angina pectoris, coronary occlusion (not coronary thrombosis) and congestive heart failure. Other types of heart disease or of vascular disease may be present, in particular arteriosclerosis of aorta or of coronary arteries, chronic rheumatic valvular disease, hypertension, and uncommonly subacute bacterial endocarditis. A confusing picture is sometimes presented by the aorta when syphilis and atheroma are present together this not infrequently happens in older patients. Syphilitic aortitis predisposes to sclerosis, elongation, and tortuosity of the aorta, but apparently not much to dissecting aneurysms. Pericarditis is a rare complication of aortitis and is not a part of the syphilitic picture *Important cardiac arrhythmias are also uncommon*, especially atrial fibrillation. Premature beats are occasionally seen and are frequently followed by pulsus alternans if the left ventricle is weak. Heart block, either atrioventricular or intraventricular in type, is found now and then but it is rarely of high grade complete atrioventricular block and bundle branch block are much more commonly the result of nonsyphilitic coronary disease.

Central nervous system syphilis complicates cardiovascular syphilis in from 20 to 30 per cent of the cases, while cardiovascular syphilis has been reported in 20 to 25 per cent of cases of general paresis and in from 15 to 50 per cent of cases of tabes dorsalis.

Treatment. With the advent of penicillin the discussion of the treatment of cardiovascular syphilis needs radical revision. It resembles that of subacute bacterial endocarditis in that a really specific and curative therapy of the active disease process has been introduced though leaving behind it, as in the case of subacute bacterial endocarditis too, a scarred heart, but it differed markedly in the past in that there already existed for cardiovascular syphilis

reasonably good therapy Although penicillin may eventually completely re place the heavy metals, namely arsenic, bismuth, and mercury in the treat ment both of syphilis initially and of its sequel of cardiovascular disease, I shall retain here, for use even if only supplementary and for historic interest during transition, much of the detail of the therapy presented in the last edition of this book.

Current experience has established the value and safety of penicillin therapy of cardiovascular syphilis and therefore such treatment is more and more replacing that with the heavy metals. At first it was feared that the speedy resolution of the active disease in aorta and heart might have serious consequences in the way of weakening the wall and of inducing the Jarisch-Herxheimer reaction. Hence at first very small doses of penicillin were ad ministered, for example, 500 to 5 000 units, but as time went on it was discovered that much larger amounts could be safely and effectively given, 25,000 to 100,000 units (Tucker and Farmer 1947 Moore et al., 1948 Kossmann and Flaum 1948 Porter 1948) But apparently the coexistence of neurosyphilis, especially general paresis, does increase the threat of the Herxheimer reaction (Moore, et al 1948) Several authorities have recommended for the adequate treatment of cardiovascular syphilis a total dosage of from 5,000,000 to 15 000,000 units of sodium penicillin given in aqueous solution by intramuscular injection over a period of about three weeks, for example, 40,000 units every three hours for 150 doses (Kossmann and Flaum, 1948) Procaine penicillin in the dosage of 600,000 units once daily in the buttocks or 300 000 units twice daily for ten days to two weeks can be more conveniently administered.

For particular symptoms special treatment is indicated, as in the use of the nitrites for angina pectoris, or digitalis and, if necessary diuretics for congestive failure, and of hypnotics and narcotics for insomnia and aneurysmal pressure pains. For intractable angina pectoris and pains due to pressure or erosion by an aneurysm, paravertebral sympathectomy or alcohol injection has proved of much value (see Chapter 21) Total thyroidectomy is contraindicated.

It is regarding specific antisyphilitic therapy with the heavy metals that there was much disagreement in the past. Some were for forcing it vigorously in the hope of stopping the progress of the disease, others would give none for fear of weakening the aortic wall or myocardium by too rapid a destruction of treponemata and resolution of inflammatory tissue, with resultant heart failure or increased stretching of aortic wall. The wisest course undoubtedly rested between these two extremes—namely the careful long-continued ad ministration of a moderate amount of antisyphilitic drugs, determined in each individual case by the condition and needs of that case. In the presence of congestive failure antisyphilitic therapy was withheld until treatment of the failure had been successful, but today penicillin can be given concurrently under careful supervision.

The technic in the use of the heavy metals which has been successful in

many cases of cardiovascular syphilis in the past may best be quoted directly from the several paragraphs concerned in the last edition (1944) of this book. The only debatable point concerns the addition of potassium iodide which, although traditional, has been omitted by a number of authorities without detracting from the success of the treatment. Incidentally it has not been necessary to add potassium iodide to penicillin in the new therapy of syphilis. It seems reasonable, therefore, to place in brackets the reference to potassium iodide in the quoted paragraphs.

"The following procedures for the administration of specific therapy in cardiovascular syphilis, although by no means the only methods that may be employed, have proved by extensive experience to be satisfactory. If the diagnosis is certain or reasonably sure and congestive failure or serious renal and hepatic disease are not present, therapy is begun with mercury or preferably bismuth, and potassium iodide. It is preferable to begin with bismuth, in the form of an insoluble salt (the subsalicylate) by intramuscular injection, in the dosage of 0.1 gram (1½ grains) every four days for four weeks and then 0.2 gram (3 grains) weekly for another eight weeks. [Simultaneously with the bismuth, potassium iodide should be given by mouth, 2.0 to 3.0 grams (30 to 45 grains) three times daily.] The drugs must be decreased in dosage or stopped if toxic symptoms arise; such toxic symptoms consist chiefly of salivation in the case of bismuth [and of urticaria, erythema, lachrymation, and coryza in the case of potassium iodide]. Also there must be a pause in the specific antisyphilitic therapy if congestive heart failure supervenes, except that either of the two excellent mercury diuretics, Salyrgan (Mersalyl) or Mercupurin (Novurit) may be injected intravenously or intramuscularly in the dosage of 2 cc. weekly or once every few days until the congestion is cleared up; such therapy acts, however, in combating the heart failure rather than in controlling the cardiovascular syphilis.

At the end of this first course of twelve weeks, arsenic should be cautiously added to the therapy if the condition of the patient warrants, as it usually does. Mapharsen in twelve weekly intravenous injections, beginning with 0.02 gram and increasing gradually to a maximum dose of 0.04 gram, is desirable if possible. Bismarsen (bismuth arsphenamine sulphonate) may be given, instead of Mapharsen, to the less favorable, that is, the sicker patients, by intramuscular injection of 0.1 gram every five days increasing to 0.2 gram at a dose for a period of twelve weeks.

At the end of this second course, one should return without pause to the therapy used in the first course, injections of an insoluble bismuth salt [along with potassium iodide]. These two courses should then be alternated every three months for a minimum period of two years. After that, one course of bismuth followed by one course of Mapharsen or Bismarsen should be given annually for the duration of the patient's life.

"Such antisyphilitic therapy as has been outlined above may now and then yield striking results, with decrease or disappearance of angina pectoris or of heart block, or with cessation of growth or even decrease in size of aorta or aneurysm. In many cases it merely retards the progress of the disease. Rarely it does harm but discrimination in the selection and administration of the therapy obviates almost all danger. Taking everything into consideration, prolonged but not rapid specific

therapy of cardiovascular syphilis is well worth while. Not only is life prolonged by adequate therapy (by several years in Moore's series of cases of aortic aneurysm and syphilitic aortic regurgitation, as compared with control cases—Moore, et al., 1932, and Padget and Moore, 1935) but symptoms are decreased and disability is lessened.

The most important consideration of all, however with respect to cardiovascular syphilis is that it is a preventable disease, early and thorough treatment of the initial syphilitic infection should practically wipe out syphilitic aortitis and its sequelae.

Differential diagnosis. Cardiovascular syphilis, chiefly in the form of aortitis, *is to be differentiated particularly from angina pectoris of nonsyphilitic origin,* from chronic valvular disease of rheumatic nature especially affecting the aortic valve, from a kinked or tortuous aorta due to extensive atherosclerosis or to a high position of the diaphragm with horizontally placed heart simulating a dilated aorta in the roentgenologic anteroposterior view but easily identified in the oblique views, from mediastinal tumors which may simulate aortic dilatation or aneurysm by physical examination and roentgen ray and from hypertensive arteriosclerotic heart disease with aortic dilatation, aortic regurgitation, and congestive failure. Very rarely there may exist acute gummatous myocarditis simulating acute myocardial infarction (Reifenstein, 1936) All signs and symptoms, including the Wassermann and Hinton reactions, must often be considered together before a definite diagnosis can be arrived at; sometimes even then it is impossible to differentiate syphilitic aortitis from these other conditions. The only fairly certain sign is that of the presence of an aneurysm of the thoracic aorta in the male aneurysms of the abdominal aorta are generally arteriosclerotic, as are also rare thoracic aneurysms in old women. The earliest stage of aortitis cannot be diagnosed clinically the aorta being at that time of normal size and shape.

Aortic syphilis has been and in fact is still being overdiagnosed in the presence of the combination of angina pectoris or aortic regurgitation and of a positive serologic reaction or a history of syphilitic infection. In truth angina pectoris is uncommonly due to syphilis, even though syphilis is present in the case and also in some parts of the world where rheumatic heart disease is common, rheumatic aortic regurgitation and syphilis, with or without aortitis, may be present in the same patient.

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CHAPTER 17

THE HEART IN DIPHTHERIA, SCARLET FEVER, AND TUBERCULOSIS AND IN OTHER BACTERIAL INFECTIONS INFESTATIONS, AND VIRUS DISEASES

Although this chapter is steadily shrinking in importance in the overall picture of cardiovascular disease because of current improvement in the control of infectious diseases both prophylactically and therapeutically throughout the world, our knowledge of the cardiovascular effects of many diseases has widened and deepened during the last generation as in the case of the virus diseases.

Two or three generations ago the bulk of all heart disease was blamed on infections many cases were rightly so labeled but many more were incorrectly diagnosed, particularly those with unrecognized congenital, hypertensive, and coronary heart disease Now infectious cardiovascular defects are known to comprise but a minority of all cases of clinical heart disease one reason for this change in viewpoint is the actual decrease in certain serious infections that can cause primary damage to the circulation, but the more significant reason is the correction of the old-time exaggerated point of view It is true, however that many diseases which may be fatal show changes in the heart that are terminal in nature though not present in serious degree during life and that even the infections which do not directly cause heart disease can be serious or fatal complications in cardiac cases so that their control does have an important effect on the longevity of persons with heart disease. An interesting comparison of the standardized death rates per 100 000 among insured persons aged 1 to 74 years in this country in the years 1917 1941 and 1948 has recently been made possible (*Statistical Bulletin* Metropolitan Life Insurance Company March, 1942, Vol. 23 No 3 Dublin, personal communication, 1949) diphtheria in 1917 showed a rate of 21 7 in 1941 only 0.7 and 0.4 in 1948 syphilis 19 1 in 1917 9 1 in 1941 and 4 8 in 1948 pneumonia (all forms) 131 8 in 1917 23 0 in 1941 and 15 2 in 1948 typhoid

fever 12.0 in 1917 0 8 in 1941 and 0 1 in 1948 and tuberculosis (all forms) 202.2 in 1917 40.9 in 1941 and 25 9 in 1948.

Having considered in the last three chapters the more important cardiovascular infections, rheumatic, acute and subacute bacterial, and syphilitic, we turn now to other infections which have a relatively uncommon or unimportant effect on the heart. Only occasionally do a few of these infections cause serious heart disease.

DIPHTHERIA

Diphtheria, during and following World War II, has had a recrudescence of importance because of its increased frequency in the wake of the hardships in Europe and Asia and of its protean form among the military forces of the U.S.A. It often causes important damage to the heart muscle but happily it has been robbed of so much of its threat in recent years by large scale prevention of the disease in the first place, and, secondly when it does occur by the use of antitoxin, that much less diphtheritic heart disease is nowadays diagnosed than was the rule a generation ago During World War II nonfaucial diphtheria was on occasion unrecognized when it attacked other parts of the body especially the skin, and serious cardiac effects were at times noted before a correct diagnosis was made.

Pathology The acute effect of severe diphtheria which is not quickly or sufficiently combated by antitoxin may be serious. There is clear evidence that grave myocardial damage may occur and that this may lead to death. The diphtheria bacillus itself is rarely encountered in the heart, it acts evidently through the toxin it produces, which, circulating in the blood stream, reaches the heart muscle. The necrosis (Figure 90) produced in the myocardium may be found only at postmortem examination, or it may give evidence during life by the production of various grades of atrioventricular or intraventricular block (shown by electrocardiogram) or rarely of heart failure. In some cases there may be multiple small hemorrhages throughout the heart as well as in other parts of the body (as in the liver and intestines) and it seems likely that such hemorrhages in the heart muscle may play some role in the sickest cases. Undoubtedly death during diphtheria results from the myocardial involvement in a considerable percentage of the fatal cases such death may come abruptly without warning, or after giving evidence such as that noted above. Endocarditis and pericarditis are not caused by diphtheria except in unique cases (Sutherland and Willis, 1936)

There is very infrequently any clinical evidence of a chronic effect on the heart from diphtheria, even when it has been severe. Survival usually means escape from any permanent or serious heart disease. Slight lesions which may be discovered by microscopic examination of the myocardium doubtless occur in some cases but they are not demonstrable by clinical examination. Therefore it is reasonable to infer that any serious sequelae are absent rather than present. Rare cases of chronic atrioventricular or intraventricular heart block

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but weakness and listlessness are the commonest symptoms accompanying the cardiac involvement, and these may be due rather to the general effect of diphtheria on the whole body (nervous system, vasomotor control, and musculature) than to the cardiac involvement. With the rare complication of congestive heart failure cough may appear

Signs. Signs also are relatively infrequent. There may appear pallor cyanosis, cardiac enlargement due to dilatation, tachycardia, diastolic gallop rhythm (which may be due either to delayed atrioventricular conduction or to cardiac dilatation and failure, or to both) an apical systolic murmur due to secondary mitral regurgitation, or an arrhythmia, which may include an ominous ventricular paroxysmal tachycardia, and rarely bradycardia, due to heart block. There may be hepatic engorgement and tenderness, and pulmonary râles due to heart failure If a majority of these signs are present the immediate prognosis is very serious.

Fever is not a sign of diphtheritic myocardial involvement, in fact the most serious heart trouble exists after the fever of the acute illness is over Fluoroscopic examination, if such can be safely undertaken, may show dilatation of the heart. Electrocardiographic examination is of greater value than any other special method, by revealing the degree of atrioventricular or intraventricular (bundle branch) block or more commonly abnormalities of the *T* wave. Blood and urine examinations and other such studies are not of much help

Course and prognosis. When involvement of the heart in diphtheria reveals itself by signs or symptoms the course of the illness is short and fatal or long and exhausting with the prognosis in doubt. Although about half of such cases recover they are not out of danger for weeks and they may die suddenly at any time during this period of convalescence Heart block is usually a fatal sign, especially bundle branch block. A follow-up study of cases of diphtheria at the South Department of the Boston City Hospital has revealed a few survivors after the development of atrioventricular or intraventricular block. On recovery from the diphtheria, such cases have lost all electrocardiographic evidence of heart block except for very rare individuals who retained some degree of atrioventricular block: there were none in this particular series in whom intraventricular (bundle branch) block persisted (Faulkner and Place, personal communication) though one such case was reported by Perry (1939) *T* wave changes also tend to clear up, although rarely inversion of this wave in Lead 1 or Lead 2 has persisted for a few months or even a few years.

Complications. Heart block and cardiac dilatation have been mentioned as grave cardiovascular complications of diphtheria. There are two other serious cardiovascular complications, difficult to analyze, namely vagal and splanchnic paralyses. The tachycardia in diphtheria has sometimes been ascribed to vagal paralysis, resulting from damage to this nerve by the diphtheritic toxin, and also to circulatory failure from vasomotor (splanchnic) paralysis the latter has also been blamed for some of the deaths. It seems

probable that these are real factors how responsible they may be as compared to actual myocarditis we do not know it is probable that all these factors operate simultaneously in a seriously sick patient.

Treatment. In the first place adequate antitoxin should be given at the onset of the diphtheria the more severe the illness, the more units of antitoxin should be administered, even up to 50 000 or 100 000 This early therapy is the most important of all measures to protect the heart. Rest in bed should be enforced for at least several days after all signs of infection have gone, even in the mildest cases, and for several weeks in the severe cases, especially if there have been symptoms or signs of cardiac involvement. For serious cardiovascular complications, absolute rest and intravenous dextrose (glucose) injections (25 to 100 cc of 50 per cent solution daily or oftener) have been found more helpful than other measures. Digitalis, epinephrine (adrenaline) and other stimulating drugs, with the possible exception of caffeine and theophylline ethylene diamine (aminophyllin) have been disappointingly ineffective in the treatment of cardiac failure and vasomotor collapse in diphtheria, early adequate treatment of the infection itself will prevent such complications.

Differential diagnosis. The differential diagnosis of diphtheritic heart disease is usually not difficult. It must be distinguished from the unimportant neurocirculatory asthenia (effort syndrome) that may come in diphtheria as in any infectious disease, from the tachycardia due to vagal paralysis, and from coincident heart disease, such as rheumatic valvular disease. It must be borne in mind also that diphtheria of the skin or mucous membranes other than of the fauces can result in serious heart disease.

SCARLET FEVER

There is, strictly speaking, probably no such entity as the "scarlet fever heart" although there may occasionally occur temporary toxic cardiac effect. Permanent heart disease certainly does, however follow scarlet fever in rather rare cases. Evidence that has been accumulating in the past few years indicates that scarlet fever like certain other streptococcus infections, merely plays the role of an activating agent of the rheumatic infection in the heart in individuals who belong to "rheumatic families" (Paul, Salinger and Zager 1934 Faulkner Place and Ohler 1935) Further important evidence that scarlet fever per se does not cause any important myocardial disease has been advanced by Shookhoff and Taran (1931) who found in the electrocardiograms of fifty consecutive patients with scarlet fever only minor changes in the *T* waves or *Q-T* intervals in 10 per cent and no prolongation of the *P-R* interval in any case, in contrast to the frequent changes, especially prolongation of the *P R* interval, in acute rheumatic heart disease. The statistical evidence which we possess at present indicates that not over 0.5 per cent of all cases of scarlet fever are complicated by endocarditis or pericarditis or both, and that a very small fraction of 1 per cent of cases of heart disease originate during scarlet fever The chronic valvular disease that results is of rheumatic type

but it does not ordinarily develop to the stage of marked valve deformity The mitral is the valve ordinarily attacked, the aortic rarely In a series of 602 cases of scarlet fever observed during one year (August, 1943 to August, 1944) 36 (6 per cent) showed cardiac complications during the acute illness 32 with myocarditis, of whom one died with atrial fibrillation and two others showed partial a-v block and 4 with endocarditis (Neubauer 1945)

It is especially in patients in whom acute polyarthritis complicates scarlet fever that acute cardiac infection tends to occur valvular disease has, however, also been reported in scarlet fever with no arthritis. It is important always to wait until the completion of convalescence before ascribing to valvular damage an apical systolic murmur which may be merely a temporary accompaniment of the scarlet fever itself More than half of the cases of acute endocarditis or pericarditis occurring in scarlet fever show an arthritis at the onset of the heart disease.

The pathologic changes are similar to those of rheumatic heart disease, both in the acute and in the chronic stages.

There are no symptoms of the heart involvement itself except for a slight prolongation of the fever and occasionally pain from pericarditis.

The only signs are the development of slight cardiac enlargement and of heart murmurs, rarely the occurrence of a pericardial friction rub, during or at the end of the scarlet fever and minor electrocardiographic changes noted above.

The treatment of scarlet fever and therefore favoring the prevention of the infrequent heart disease that results, has been improved since the introduction of penicillin which should be administered at the very onset of the hemolytic streptococcus sore throat which ushers in the scarlet fever and continued until convalescence begins, in order to prevent especially the formerly serious and common complication of mastoiditis.

The differential diagnosis is inconsequent, in that the acute heart disease, with or without pericarditis, occurring during scarlet fever and the chronic valvular disease that may follow are indistinguishable from rheumatic heart disease, acute and chronic.

STREPTOCOCCUS HEMOLYTICUS INFECTION WITH HEMORRHAGIC NEPHRITIS

Among others, Whitehill, Longcope, and Williams (1939) have called attention to this serious disease in childhood which is not infrequently attended by a complication of cardiac dilatation and even heart failure early in the illness (71 per cent of the series of 138 cases of Whitehill, et al.) but fortunately nowadays penicillin given as near the onset of the disease as possible can result in much improvement and may help to prevent the more serious cardiac effects, provided the streptococcus infection itself is still active the penicillin does not cure the nephritis itself. The death rate used to be fairly high (20.3 per cent of the 59 severe cases in the series just mentioned) recovery was

slow but the heart did often return to normal (see also Chapter 23) Happily the picture has changed and this disease should be on the way out.

PNEUMONIA

Pneumonia, either lobar or bronchial in type, may prove a great strain for an already weakened or diseased heart, but it does not itself cause serious heart disease except in rare instances when acute bacterial (generally pneumococcus) endocarditis or a septic pericarditis occurs, in either case almost always a fatal complication in the days before chemotherapy with the sulfonamide drugs and the introduction of the antibiotics, especially penicillin, but this complication is now largely preventable and most cases that do occur are curable by the use of these drugs (formerly sulfadiazine, sulfathiazole, or *sulfapyridine 1 to 2 gm 15 to 30 gr 3 or 4 times a day for a few days,* under careful observation and with blood titration, and now preferably procaine penicillin by intramuscular injection, 300 000 units daily for a few days to a week, or terramycin, chloromycetin, or aureomycin by mouth about 500 mg every 6 hours for a week) The various antibiotics should be appraised as to their efficacy by direct testing on the growth of the responsible organisms themselves.

Electrocardiograms in the course of and immediately following, severe pneumonia may show various arrhythmias and sometimes important changes such as inversion of the *T* waves and prolongation of the *P R* interval, the more severe the disease the more marked the changes, but these abnormalities subside during convalescence. Undoubtedly they are to be ascribed to a direct toxic effect on the myocardium (Cohn and Jamieson 1917 Master et al 1931) At postmortem examination the heart muscle cells may show cloudy swelling, but such a finding does not constitute real heart disease.

As will be observed concerning typhoid fever and exanthematic typhus, the weakness and collapse due to pneumonia are not the result of cardiac failure but of the infection. It is, therefore, not to be expected that routine digitalis therapy in pneumonia should help except when there is obvious congestive failure or a rare complication such as atrial fibrillation or atrial flutter

TYPHOID FEVER

The rare invasion of the endocardium by the typhoid bacillus producing acute or subacute bacterial endocarditis has already been mentioned (Chapter 15) Much more common but of little or no clinical importance, is the finding at postmortem examination of slight to moderate, scattered, toxic changes of muscle fibers and interstitial tissue, consisting of cloudy swelling and infiltration with small round cells, in the majority of cases dying of typhoid fever Also periarteritis and endarteritis have been found in the blood vessels of such patients, even to the extent of causing ulceration and aneurysm of the aorta. Pericarditis is a rare complication.

Generally the heart is not affected to any important or appreciable degree

in typhoid fever Not infrequently however *T* wave changes (flattening or inversion) and rarely delayed atrioventricular conduction can be found by electrocardiogram during the acute infection, but no high degree of block (Brow 1929 Porter and Bloom 1935 Mainzer 1947) and if cardiovascular symptoms occur they are in the nature of the effort syndrome usually found in infectious disease Of course organic heart disease of other nature may happen to complicate and be overburdened by the infection, but it is wrong to treat the heart with digitalis or other such drug in order to combat the symptoms of effort syndrome or of circulatory failure due to vasomotor paresis. It is apparently not heart failure that kills in typhoid fever but the toxic effect with weakness and vascular collapse resulting from the infection. Also avitaminosis associated with the malnutrition during a prolonged illness with typhoid fever may play a role electrocardiographically and otherwise (Rachmilewitz and Braun, 1948)

TUBERCULOSIS

Tuberculosis does not cause heart disease itself except in rare cases in which there is direct tuberculous invasion of the myocardium or endocardium. Pericardial tuberculosis is, however occasionally encountered as either (1) an isolated lesion, (2) a part of a polyserositis, or (3) an extension from mediastinal tuberculosis.

Tuberculosis of the myocardium is infrequently found at postmortem examination as a part of a miliary tuberculous process or in the form of a solitary tubercle or abscess. It is an autopsy finding, rarely even suspected during life. The miliary tubercles in the heart muscle almost never produce any symptoms or signs, the illness being that usually observed in miliary tuberculosis. If invasion or pressure directly involves the atrioventricular conduction system, heart block may occur with arrhythmia and slow pulse, or myocardial tuberculosis may even cause congestive heart failure (Wilbur 1938 also personal observation, 1947) Still more rare than disease of the heart muscle in miliary tuberculosis is a myocardial invasion by a solitary tubercle or tuberculous (cold) abscess such invasion is usually symptomless and without signs but it is capable of causing an aneurysm of the heart wall which may even lead to rupture and to death. In a series of 7 683 cases of tuberculosis, myocardial tuberculosis was found 49 times (0.63 per cent) (Raviart, 1906)

Tuberculous endocarditis is also rare, infrequent cases, usually of miliary tuberculosis, revealing at autopsy tubercles in the endocardium of the heart walls and of the valves, or tuberculous ulceration of the endocardium. Tubercle bacilli have been found in such endocardial lesions. There is no evidence that chronic valvular disease can originate either directly from tuberculous inflammation or indirectly from the toxic effect of tuberculosis elsewhere in the body

Tuberculous pericarditis is not rare. It is an important type of acute and also of chronic pericardial disease isolated or more commonly associated

with a similar involvement of pleura or with a tuberculous involvement of the mediastinum arising from lymphatic glands, spinal caries, or other cause. It is not usually accompanied by myocardial or endocardial tuberculosis, but in rare cases, for example, in miliary tuberculosis, it may be thus complicated. Isolated tuberculosis of the pericardium, unsuspected during life, has been discovered to be an occasional cause of death in elderly individuals (Thompson, 1933)

Pericardial effusion is a common accompaniment of pericardial tuberculosis and may be very slow and insidious in its onset, causing few or no symptoms at first but finally incapacitating the patient by its pressure effect, which prevents adequate filling of the heart (cardiac tamponade—see Chapter 27) or by associated fever and weakness. The effusion, often, in fact usually hemorrhagic in character may develop to enormous size (even up to 2 or 3 liters) and because of its very gradual growth may be astonishingly well supported for a long time, even for many weeks It is much better endured by the patient than is the more acute rheumatic pericardial effusion of the same amount of fluid. The tuberculous effusion may be spontaneously absorbed, or with the development of serious symptoms and signs, require paracentesis. The symptoms—dyspnea, cough, and oppression—come from pressure effects and but rarely include sharp pains such as are frequent in rheumatic pericarditis. The signs are those of a small, moderate, or large accumulation of fluid in the pericardium with slight, moderate, or enormous increase of the area of percussion dullness over the heart and of the roentgen ray shadow. With a large effusion the arterial blood pressure is low especially the pulse pressure, there is often a well-marked paradoxical pulse, and the systemic venous pressure is elevated with resulting prominence of the jugular veins and pulse and enlargement of the liver: these are signs of acute or subacute constrictive pericarditis (the so-called cardiac tamponade) A pericardial friction rub may be heard over the precordium even in the presence of a large effusion.

After the subsidence of the acute process a serious chronic pericarditis may develop frequently with involvement of the mediastinum If extensive this chronic mediastinopericarditis may so cramp the heart chambers and great veins that the entrance of blood into the heart is obstructed. Generally the obstruction is most manifest in the hepatic veins with resulting hepatic engorgement and ascites this condition has, therefore been called chronic mediastinopericarditic pseudocirrhosis of the liver or Pick's disease (Chevers, 184 Pick, 1896) but a better designation is chronic constrictive pericarditis (see Chapter 27) Sometimes the process may be slight, without handicap from the nonconstricting or only slightly constricting pericardial adhesions.

Tuberculosis of the blood vessels may occur in rare instances, causing endarteritis, granulomata, and even aneurysmal dilatations. The invasion may be either from the blood stream or from infected tissue (lymph nodes, for example) contiguous to aorta or other blood vessel.

The introduction of streptomycin has given promise of aid in a few instances of tuberculous pericarditis this drug in the dosage of 2 to 4 gm daily

has been apparently helpful, but its toxic effects are a distinct drawback (see page 403 in Chapter 15)

The relationship of heart disease to tuberculosis of the lungs. It has long been said that pulmonary tuberculosis is rare if there is considerable mitral stenosis. This appears to be true; the reason is not clear but it may be that the chronic pulmonary congestion resulting from mitral stenosis makes it difficult for the tubercle bacillus to gain a foothold. In one series of 300 cases of mitral stenosis there was found but one case of pulmonary tuberculosis (0 3 per cent) and in a series of 20 000 cases of pulmonary tuberculosis there was reported to be but one case of mitral stenosis (0 005 per cent) (Montenegro 1919) Valvular heart disease of other sort (not marked mitral stenosis) is, however occasionally and incidentally seen in pulmonary tuberculosis the combination was reported in 29 out of 1 097 cases of pulmonary tuberculosis, valvular heart disease or both, examined post mortem (Calthrop 1920) in 31 out of a series of 13 000 cases of pulmonary tuberculosis (Kellner 1921) and in 0 9 per cent of 7 115 necropsies on tuberculous patients (Brown, quoted by Hawes 1932) An analysis of 522 adults with pulmonary tuberculosis revealed 3 cases of rheumatic heart disease and 2 of congenital heart disease (Buckingham and Hoffman, 1935)

In contrast to the rarity of pulmonary tuberculosis in cases of pronounced mitral stenosis it is said to be rather a usual development in congenital stenosis of the pulmonary orifice (Austrian, 1933) In this regard it is of interest that just the opposite conditions exist in the pulmonary circulation with these two lesions in mitral stenosis the pulmonary circulation is engorged and in pulmonary stenosis it is depleted.

Much more important than the possible protective action of mitral stenosis in the case of phthisis is, in rare cases, the deleterious effect of extensive pulmonary tuberculosis on the heart. This is not the production of the familiar so-called drop or vertical (or "atrophied") heart, which is sometimes seen in the more slender victims of tuberculosis with low diaphragm and general atonic state such a drop heart is of little or no importance in itself Rather is it the strain on the right ventricle resulting from increased pressure produced in the pulmonary circulation by obstruction caused by extensive destruction of pulmonary tissue, fibrosis, and pleural adhesions. This strain may eventually in a few cases produce some right ventricular enlargement, rarely to a considerable degree and not marked enough to cause definite increase beyond the normal in the percussion or roentgen ray size of the heart, so that the change may easily escape notice In a very few cases actual failure of the right ventricle may occur but this is much rarer than in the case of chronic pulmonary fibrosis and emphysema of other cause, which will be discussed in Chapter 20 During life there may be a great variety of size and shape of the heart shadow in the presence of active pulmonary tuberculosis (Porter and Gordon, 1937)

Finally it is to be recognized that in patients with active tuberculosis in the lungs or elsewhere there is commonly as in the case of other infections,

a certain degree of neurocirculatory asthenia, with dyspnea, palpitation, and heartache, which may on hasty analysis be wrongly ascribed to heart disease or to a toxic effect of tuberculosis of the heart.

The course prognosis, and treatment of tuberculosis of the heart and pericardium resolve themselves primarily into those of the underlying tuberculosis, be it miliary pulmonary or of the nature of polyserositis. The prognosis is always grave, though some cases recover: this number has increased somewhat since the introduction of streptomycin. A pericardial effusion may need to be tapped and cases of chronic constrictive pericarditis may require surgical relief by pericardial resection. Active tuberculosis of pericardium and heart must be treated by rest and good nursing care and a trial of streptomycin, just as in the case of active pulmonary tuberculosis, but the prognosis is always serious.

EPIDEMIC CEREBROSPINAL MENINGITIS

Meningococcus infection may in rare cases involve the heart and cause an acute bacterial endocarditis or pericarditis, as noted in Chapter 15 but such cardiac involvement is now largely preventable or amenable to recovery by *the use of chemotherapy Meningococcic myocarditis has also been reported* (Saphir 1936)

GONORRHEAL INFECTION

Acute or chronic gonorrhea may in rare cases infect the heart, especially following gonorrheal arthritis or a virulent illness of other nature due to the same organism The involvement occurs in the form either of acute or of subacute bacterial endocarditis and is no longer as it once was, fatal, the newer chemotherapy being a specific remedy in most cases.

OTHER BACTERIAL DISEASES INCLUDING SEPTIC INFECTIONS

Erysipelas, septic infections, and pyemia due to streptococcus or staphylococcus used to be occasional causes of acute bacterial endocarditis, septic (purulent) pericarditis, and myocardial abscesses Generally these were but terminal manifestations and were not responsible for death, but sometimes they constituted the chief or most important part of the disease. Treatment used to be of little avail when the heart itself was diseased but both prevention and recovery of cardiac and pericardial complications now may follow the use of the antibiotics (especially penicillin) and of the sulfonamide drugs, aided by pericardiotomy and drainage in the case of purulent pericarditis.

RICKETTSIAL DISEASES

Typhus fever Myocardial lesions and vascular disease (endarteritis) may result from exanthematic typhus, fortunately now rare in civilized countries at peace: they are as a rule of little or no significance. Transient *T* wave ab-

normalities in the electrocardiogram are common during the acute infection (Norvilt, 1947) Complete arterial obstruction and gangrene may however complicate a few cases. The toxicity and vasomotor paralysis resulting from this infection may kill, but involvement of the heart is probably not responsible for death. Endocarditis and pericarditis do not occur except from a secondary infection.

Another important rickettsial disease which has been found even more constantly to be associated with myocardial involvement, namely *tsutsugamuschi fever* or *scrub typhus* was studied during World War II A large proportion of electrocardiograms of cases of scrub typhus has shown abnormalities chiefly in the *T* waves with recovery in most cases.

Rocky Mountain spotted fever also falls into the group of rickettsial diseases and may affect the myocardium during the acute illness.

VIRUS DISEASES

An interesting and important advance in our knowledge of the effect of infections on the heart has taken place during recent years in the field of the virus diseases. In most instances the victims of such infections escape any serious cardiac injury but in a certain number of instances, rare as a rule, the myocardium may be seriously affected. Virus pericarditis has also of late been identified.

Influenza had long been suspected and by some so incriminated, but only in the last few years has actual proof been presented (Finland, et al., 1945) It is quite possible that lesser lesions of the heart muscle have often resulted from influenza but serious or fatal myocarditis is rare. Most of the symptoms which years ago were attributed to such a condition were characteristically those of a fatigued state or neurocirculatory asthenia which so often complicates the convalescence from any infection (see Chapter 22)

Mumps has been shown to produce temporary atrioventricular block in rare cases, clearing with convalescence (Rosenberg, 1945)

German measles (rubella) has been shown to have in many instances a serious effect on the eyes and heart of a fetus if it attacks the mother during the first three months of pregnancy (Gregg, 1941 Swan, 1943)

Yellow fever may give rise to nonspecific myocardial inflammation and degeneration in fatal cases (Cannell 1928)

Poliomyelitis. Recently myocardial changes characterized by *perivascular* infiltration of lymphocytes and neutrophiles have been reported in 6 out of 7 cases with poliomyelitis who died suddenly during the acute or convalescent stages (Saphir and Wile 1942) and several other observers have confirmed these findings since (Gefter et al., 1947 Ludden and Edwards, 1948)

Infectious hepatitis and *infectious mononucleosis* have also been found to cause in some cases myocardial involvement as indicated electrocardiographically

Still other viruses need further appraisal in this respect.

TRICHINIASIS

It was long known that trichiniasis may involve the myocardium as well as other muscles in the body but the possible frequency with which the trichinae invade the heart in well-infested cases was not pointed out until 1935 (Spink, 1935) A serious effect directly from this heart involvement itself has not been found, but changes in the electrocardiogram (flattening or inversion of the *T* waves, low voltage of *QRS* waves, and intraventricular block) in some cases (6 of 18 patients with myocardial trichiniasis in Spink's series) may justifiably be attributed to the presence of the parasites in the heart muscle. In another series of 44 cases of trichiniasis of mild type however only 2 showed possible clinical evidence of myocardial involvement (Beecher and Amidon, 1938) There is no specific therapy

TRYPANOSOMIASIS

A cause of heart disease in South America (especially in Brazil) rare or nonexistent elsewhere namely cardiac trypanosomiasis, has been frequently reported in recent years following its discovery in human beings by Chagas in 1909 This consists of the invasion of the myocardium in childhood by trypanosomes (Figure 91 illustration below) with foci of inflammatory reaction, which later lead to cardiac weakness and failure and arrhythmias in



FIG. 91 Microphotograph showing myocardial trypanosomiasis (Chagas' disease) Note Trypanosoma cruzi near the center of the field. (Kindness of Drs. C. Chagas and R. Menezes, Brazil, and Frank Wilson, Ann Arbor Michigan.)

middle life. Sudden death may result. The pericardium, endocardium, and valves are not involved, but the myocardium is said to be more often involved than in any other disease. In the chronic cases multiple areas of fibrosis may be found scattered through the heart muscle. Thousands of cases of this remarkable type of heart disease have been seen in Brazil, but it has not yet been encountered in the United States or Europe.

ECHINOCOCCUS DISEASE

Infection with the echinococcus may involve the heart, and a number of cases of hydatid cysts in or attached to the walls of atria and of ventricles or interventricular septum have been reported. It is usually but a part of general echinococcus disease. I have encountered such cases in Greece (1948).

ACTINOMYCOSIS

Actinomycosis of heart and pericardium is a very rare infection. Thirty years ago the case of a man 34 years old was reported with initial lesion in the esophagus and secondary invasion of the heart, pericardium, lung, and pleura; it was noted that twenty-two other cases had been described previously (Letulle and Hufnagel, 1919).

INTESTINAL PARASITES

Most of the parasites that invade the intestinal tract of man do not affect the heart; these include the roundworm (ascaris), the pinworm (oxyuris), and the ordinary tapeworms (taenia saginata and taenia solium), but the hookworm (ankylostoma) and, less commonly, the fish tapeworm (dibothriocephalus latus) may by their production of severe anemia cause an important degree of cardiac dilatation and loud murmurs (see Chapter 23).

OTHER INFECTIONS AND INFESTATIONS

A few other diseases may involve the heart, for example, Brucella melitensis (Malta fever), sarcosporidial infection of the myocardium, filariasis (with ova found in the heart), strongyloidiasis, cardiac heterophydiasis (infestation with flukes from raw fish), and cysticercosis of the myocardium (and brain). In the sixteenth century there were frequent reports of worms in the chambers of the human heart, before the days when it was recognized that these supposed worms were actually elongated blood clots, both ante mortem and post mortem. It is, however, true that the dog's heart may contain worms (*Dirofilaria immitis*, see Query, *J.A.M.A.*, 1924, CIII, 1728), which, introduced by insect bite, go through a cycle of development and then migrate in adult life along the veins into the right heart chambers, where by their accumulation en masse the individual thread-like filaria attaining the length of one to two feet, may actually block the circulation and cause pulmonary embolism.

Rheumatoid arthritis, periarteritis nodosa, and conditions like lupus erythe

matosus allied to these are quite frequently attended by heart disease, but it is still difficult or impossible, in view of our ignorance as to their etiology to label them as infections or even reactions to infections or toxic states (see Chapter 23)

FOCAL INFECTIONS

Focal infections may have a deleterious effect on the heart either directly or indirectly Actual cardiac disease of the nature of bacterial endocarditis is known to follow an acute focal infection like that of tonsil, of middle ear or of skin. But this happens only rarely except in the case of dental infections and extractions which almost certainly are a very important source of entry of the Streptococcus viridans into the body to inaugurate the grave infection of subacute bacterial endocarditis in cases of rheumatic or congenital heart disease (see Chapter 15) It behooves us in such cases to use the greatest vigilance in avoiding strain from too much operative work at any one time and in combating the serious results of dental and other focal infections by the use of the antibiotics (in particular penicillin) and of the sulfonamide drugs and otherwise.

How frequently slight myocardial damage or a mild endocardial lesion with recovery may occur with such focal infections we do not know but there exists no proof that this is even an occasional happening. We do know that heart disease already existing is sometimes aggravated by the presence of focal infections, with the appearance of arrhythmia or of symptoms of congestive failure or angina pectoris, or with their increase if already present. Whether or not there is actual heart disease, cardiac arrhythmia may be set off or aggravated by focal infections such arrhythmia is as a rule entirely unimportant in itself consisting of premature beats (extrasystoles) or paroxysms of tachycardia, but sometimes it may comprise atrial fibrillation or flutter or prolonged paroxysmal tachycardia Among the focal infections which may precipitate or aggravate cardiac arrhythmia, congestive failure, or angina pectoris are chronic cholecystitis, prostatitis, pyelitis, colitis, infection of gums, apical tooth abscesses, frontal sinusitis, lung abscesses, and other similar troubles.

Correction of these focal infections by surgery or by other measures (if the circulatory condition permits) may relieve the patient of his temporary state of ill health or at least cause improvement the risk of such corrective procedures is usually justified, provided too much is not attempted at one time (the removal of more than one or two infected teeth at one sitting, for example, may result in vasomotor shock, or may itself precipitate heart failure and death) The wisest course, then, is to view focal infections so far as the heart is concerned neither with overmuch fear nor with excessive disregard to consider them as possible important factors producing a state of ill health which may cause strain on the heart, and to eradicate them if possible and feasible. However it is a mistake to perform an operation of choice and not of necessity for example to remove a symptomless gallstone (or to correct surgically a

simple inguinal hernia) in the face of severe angina pectoris or of congestive failure.

INFECTIONS NOT CAUSING HEART DISEASE

Many infections never cause heart disease, although they may precipitate such trouble as failure or atrial fibrillation in hearts already diseased or they may be attended by complicating infections which do cause heart disease. This is particularly true of most of the contagious diseases of childhood whooping cough (pertussis) chickenpox (varicella) and measles (rubeola) The acute respiratory tract infections—rhinitis, sinusitis, pharyngitis, laryngitis, tracheitis, and bronchitis—do not of themselves cause heart disease, but, like tonsillitis, they may occasionally precipitate the rheumatic infection which does almost always damage the heart. The same statement is true of otitis media, but infections of the gastrointestinal and genitourinary tracts very rarely precipitate any heart trouble.

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CHAPTER 18

THE HEART IN THYROID DISEASE AND IN DISEASES OF OTHER GLANDS OF INTERNAL SECRETION

Although this chapter requires less revision since the last edition than most of the rest of the book, it is, like several other chapters, decreasing in importance and quite likely can be eliminated altogether eventually or at least demoted to a small section in the chapter on miscellaneous etiologic relationships. This is, of course, due to the constantly earlier recognition and more adequate treatment of endocrine diseases before the heart and blood vessels are importantly affected.

Endocrinopathy has very little serious effect on the heart. Even that disorder which has much more influence than any other namely thyrotoxicosis, now accounts for but a small fraction of 1 per cent of cases of heart disease in any enlightened community However there are many interesting and important cardiovascular and circulatory relationships and effects of the endocrine hormones normally and abnormally For example, the glands of internal secretion, especially the adrenal, the posterior pituitary and the thyroid, have an important influence on the distribution of water throughout the body partly by a direct effect on the kidney and cell permeability in general and partly by an effect on electrolytes and metabolism of carbohydrates, protein, and fat. The adrenal and possibly the posterior pituitary play an important role in the renal control of sodium and upon its internal distribution. Transfers of sodium and potassium across cell membranes are influenced by the hormones. And now the hormones are being studied as to their striking influence on the course of certain diseases such as rheumatoid arthritis and rheumatic fever A great deal of study remains to be done on these relationships, but they are opening up an important field which may as a matter of fact, result eventually in a considerable revision of a book such as this. Further discussions of hormonal influences will be found elsewhere in the book, for example, later in the present chapter in the discussion of adrenal diseases and in the chapters on rheumatic fever and congestive failure.

DISEASES OF THE THYROID GLAND

Diseases of the thyroid gland which materially affect the heart are only that which produces an excessive or toxic secretion (exophthalmic goiter or Graves disease) resulting in thyrotoxicosis, and that which is attended by a markedly decreased secretion (myxedema and cretinism)

Simple enlargement of the thyroid gland (colloid, or simple, or endemic goiter) causes no trouble with the heart or circulation unless the gland becomes so large that pressure on veins and arteries results in embarrassment to the entrance of blood into and its exit from the heart or compression of trachea and bronchi interferes with respiration (Rose 1878 Kocher 1902) Adenomatous goiter (struma nodosa) is much more likely to cause these disturbances than is simple colloid goiter In some parts of the world, for example in the north central ("middle west) and northwestern regions of the United States, bordering on the Great Lakes and westward to the Pacific Ocean, and in Switzerland, colloid or simple goiter with its occasional slight secondary circulatory embarrassment is common In other parts of the world, for example, in New England and in other lands bordering the sea where iodine is plentiful, such goiter is rare.

Excessive secretion is not produced by a colloid goiter but if later in life the simple colloid goiter becomes adenomatous, thyrotoxicosis may be superimposed.

THE HEART IN THYROTOXICOSIS

Thyrotoxicosis, also called hyperthyroidism may result from general hyperplasia or from adenomatous goiter The term thyrotoxicosis will be used throughout the book in the place of hyperthyroidism since it indicates a toxic degree of hyperthyroidism and includes abnormal thyroid secretion, if such exists, as well as excessive secretion.

Persistent overactivity of the thyroid gland commonly gives rise to an important but preventable type of heart trouble which has become familiarly known as the "thyroid heart, but which might better be called the "thyrotoxic heart," or the "heart in thyrotoxicosis." For the most part the heart, as well as the circulation in general, in thyrotoxicosis is simply physiologically over active, pathologic changes, that is, real heart disease, in thyrotoxicosis is relatively rare. The true "thyrocardiac" may be said to be the individual who, as a result of thyrotoxicosis, has atrial fibrillation and eventually if not properly treated, cardiac enlargement and congestive heart failure as a rule the evolution of a thyrocardiac is in just that order

Frequency Thyrotoxic heart disease varies in frequency both absolutely and relatively in different parts of the world, not only according to the frequency of thyrotoxicosis in such parts but also according to the rapidity of diagnosis and proper treatment of the thyrotoxicosis In New England 20 to 25 years ago thyrotoxicosis was found to be a causative factor in 3 per cent of

2,314 cases of organic heart disease (White and Jones, 1928) In Virginia it was reported in 3½ per cent of 300 cardiac patients (Wood, Jones, and Kimbrough, 1926) while in Oregon it was found in 11 per cent of 1,344 cardiac cases (Coffen, 1929) In Oregon there is much more endemic (colloid) goiter than in New England and Virginia, out of all proportion to the amount of thyrotoxicosis, that is, the endemic goiter is relatively much more frequent than the thyrotoxicosis That thyrotoxic heart disease is preventable and is already decreasing in communities where early diagnosis and adequate treatment of the thyrotoxicosis itself are carried out is indicated by the fact that among the first 2,500 patients whom I examined in consulting practice from 1920 to 1927 because of cardiac symptoms or signs there were 24 cases of heart disease due to thyrotoxicosis, while among the next 2,500 patients seen from 1927 to 1933 there were only 10 such cases, in the third lot of 2,500 private patients seen from 1933 to 1940 there were 4 cases, and in the fourth such series examined from 1940 to 1946 there were but 3 thyrotoxicosis not responsible for heart disease was occasionally found throughout the entire period.

Etiology *Cause* The fundamental cause of this type of heart disease is an abnormal activity of the thyroid gland with excessive (or disturbed) secretion. The mechanism by which thyrotoxicosis produces heart disease is probably dependent on three factors which may be summarized briefly as follows. First, the increased general body metabolism which results from abnormal thyroid activity increases the demand on the heart and circulation. It has been estimated that the blood flow at rest is at least 50 per cent above the normal in a case of thyrotoxicosis of average intensity and that with exercise this disproportion is still greater The increased blood flow is due not only to the increased pulse rate but also to an increase of volume output per beat from the heart, although this increase of volume output per beat is less than in a normal heart responding to exercise with the same degree of tachycardia as that found in thyrotoxicosis. The systolic blood pressure is somewhat elevated and the diastolic pressure often lowered so that the pulse pressure is frequently much increased. This constantly increased blood flow is maintained by a constant overactivity of the circulation. Such persistent overactivity tends to increase somewhat the size of the heart both in muscle (thus producing a simple work hypertrophy) and in capacity (dilatation) but cardiac enlargement is very inconstant and not the rule in the majority of cases. Eventually in some very severe prolonged cases and in those complicated by valvular heart disease, hypertension, or coronary disease, the persistent overactivity can cause excessive strain, arrhythmia, and failure. A possible parallelism has been seen in experimental animals, which show considerable cardiac enlargement after excessive exercise maintained during much of the time for weeks or months.

A second and more important consideration, however is that practically all thyrotoxic heart disease starts with a persistent atrial fibrillation the tachycardia and arrhythmia of atrial fibrillation add to the strain of the thyrotoxicosis and tend after some years to produce cardiac enlargement which might

not have occurred from atrial fibrillation in the case of a normal heart to start with, without thyrotoxicosis, particularly if the ventricular rate were adequately controlled by digitalis (an impossibility in the presence of considerable thyrotoxicosis) A third factor that helps to explain the heart disease in thyrotoxicosis is that the heart itself is the seat of specific thyroid stimulation with local increased metabolism as in the case of other tissues in the body this increased wear and tear of the cells of the myocardium favoring in its turn enlargement and failure. A fourth possible factor is that of a kind of arteriovenous shunt or aneurysm with blood rushing through the widely dilated vessels of the thyroid gland, affording an appreciable extra burden for the heart and favoring enlargement, as in the case of a traumatic arteriovenous aneurysm anywhere (Boas, 1923)

An actual myocardial lesion consisting of degenerative changes, at one time suggested as an important finding, has been in more recent years discounted and shown to be but an inconstant, incidental occurrence (McEachern and Rake, 1931 Weller and associates, 1932)

A distinction, so far as the heart is concerned, between general glandular hyperplasia and the so-called adenomatous goiter with hyperfunction (toxic adenomata) cannot be made as a rule the latter is found in older patients in whom other causes of heart strain (such as hypertension and coronary disease) are also more likely

The frequency of definite cardiac abnormality (not simply tachycardia and cardiac symptoms) in patients with thyrotoxicosis has been reported variously from a high estimate of enlargement of the heart in 50 to 60 per cent of fatal cases (McEachern and Rake, 1931 Kepler and Barnes, 1932) to a low estimate of only a few per cent in unselected groups, atrial fibrillation in about 15 per cent, and cardiac insufficiency in 5 to 10 per cent. These abnormalities of the heart are much more common when there are complicating factors like hypertension.

Age The age at which thyrotoxicosis is found varies widely from 3 years up to 76 but the commonest age of onset is from 20 to 40 years. In a series of 500 cases of thyrotoxicosis analyzed by Means and Richardson (1929) the age incidence of onset by decades was as follows first decade 3 cases, second 60 third 165 fourth 147 fifth 93 sixth 29 and seventh 3 The average age was 37 years in another series of 500 cases of thyrotoxicosis (Hurxthal, 1928) The age incidence of thyrotoxic heart symptoms parallels this more or less closely· in a series of 68 cases 56 per cent were between 30 and 50 years old (White and Jones, 1928) In a series of 108 cases of thyrotoxicosis with atrial fibrillation, the average age was 51.5 years (Barker Bohning, and Wilson, 1932) these represent the more advanced cases, on the way to serious thyrotoxic heart disease.

Sex In thyrotoxicosis itself the female sex predominates over the male the ratio is about 5 to 1 In Means and Richardson's series (1929) of 500 cases of thyrotoxicosis there were 417 females and 83 males. But the males are more severely affected and so show a relatively higher percentage of cardiac

involvement (by about 2 to 1) in a series of 34 cases of my own of thyrotoxic heart disease there were 24 women and 10 men.

Other etiologic factors Race has little to do with thyrotoxic heart disease but in days gone by social and economic status did play a role in that inadequate financial resources did at times prevent early diagnosis and surgical correction of the thyrotoxicosis and so favored the establishment of heart disease. In thyrotoxicosis itself heredity plays a part, how important we do not know

In the incidence of simple nontoxic goiter and perhaps secondarily in that of toxic goiter there is a role played by geographic factors, involving iodine content of foods and water Heart trouble due to thyrotoxicosis is more common in regions where there is much simple goiter but this is not due to the goiter itself The change of the simple goiter later in life to adenomata, which can become toxic, may account for this finding.

Finally the education and intelligence of both the lay and medical population determine the rapidity with which the thyrotoxicosis is detected and corrected—a factor of very great importance in the prevention of heart disease.

Pathology There are no constant cardiovascular lesions in thyrotoxicosis. Enlargement of the heart with hypertrophy of the fibers is present in many cases, especially in those with long-established atrial fibrillation, but it is sometimes difficult to exclude the factors of hypertensive and coronary heart disease in these cases. In a few cases necrosis of the myocardium has been found, but this finding has not been confirmed as a thyroid effect. The heart weight is generally somewhat increased, to 400 or 500 gm in serious cases the average weight of the hearts of 13 fatal cases was 438 gm, the two heaviest hearts weighing 530 gm each (Barker Bohning, and Wilson, 1932) With the onset of failure, dilatation of the cavities and atrioventricular valve rings occurs, but endocarditis and pericarditis are not found as a primary result of thyroid toxicity

Symptoms. There are no characteristic symptoms of thyrotoxic heart disease. The early cardiovascular symptoms of thyrotoxicosis itself are due to the tachycardia and effort syndrome they are chiefly palpitation and dyspnea, and uncommonly heartache. If atrial fibrillation or failure supervenes, these symptoms increase. Palpitation is of two types (1) the forceful beating with normal heart rhythm which may be extremely unpleasant, and (2) that due to paroxysmal changes in rhythm. Periods of rapid palpitation are common in thyrotoxicosis whether or not the heart is diseased, they last a few minutes to a few hours and are due to paroxysms of sinoatrial or ectopic atrial tachycardia, or of atrial fibrillation or flutter Angina pectoris rarely accompanies thyrotoxicosis, and then only in older persons in whom the stage is already set by the presence of coronary disease which is not sufficient in itself to give rise to the paroxysmal pain. The angina pectoris, like the arrhythmia and congestive failure, may be relieved by thyroidectomy when the metabolic rate is reduced thereby

Signs. Increased heart action both in rate and force is the most common

cardiovascular sign in thyrotoxicosis and this activity is manifest on inspection, palpation, and auscultation over the precordium on inspection and palpation of the arterial pulse in neck and arms, and on fluoroscopic examination. Enlargement of the heart, congestive failure, and arrhythmia, when they occur, show themselves in the usual way In the early stage of the disease the heart may at first appear to be enlarged, on hasty inspection and palpation, because of the forceful beating against the chest wall, when really it is of normal size. Cardiac hypertrophy has, however been found at autopsy in the majority of fatal cases (Friedberg and Sohval, 1937) A harsh, unusually superficial systolic murmur is sometimes heard in thyrotoxicosis in the second and third intercostal spaces just to the left of the sternum its origin is not clear but it is probably a physiologic pulmonary murmur dependent on the increased pulmonary circulation with dilatation of the pulmonary artery reinforced by the forceful heart action and thin chest wall. This pulmonary systolic murmur has in rare cases been attended by a slight thrill. Also at times a to-and-fro friction rub has been noted in the region of the pulmonary conus (Goodall, 1920 Lerman and Means, 1932) and in very rare cases a functional aortic regurgitant murmur has also been described (Parade, 1935)

Exophthalmos and thyroid gland enlargement, the most common signs of thyrotoxicosis, may be but little evident in some cases, and the heart action may first suggest the correct diagnosis. A staring or worried look is sometimes present in the absence of frank exophthalmos lid lag may be present also with little exophthalmos. Bulging of the eyes, unilateral or bilateral, may actually be precipitated or aggravated by thyroidectomy

In almost 80 per cent of cases of thyrotoxicosis the heart rhythm is normal and the pulse rate is fast, averaging 100 to 120 per minute at rest. Rare cases have a normal or only slightly elevated pulse rate. In the remaining 20 per cent the heart rhythm is disturbed, the disturbance consisting almost invariably of atrial fibrillation (noted in 207 of Ernstene s 1 000 cases, 1938) of permanent nature in two thirds of the cases and of paroxysmal type in one third. *In addition there are relatively infrequent cases with atrial flutter* and atrial paroxysmal tachycardia.

Atrial fibrillation is commonest in the cases with congestive failure, occurring in the majority of these in one series of 111 cases of thyrotoxicosis with congestive heart failure atrial fibrillation was present in 83 per cent (Hurxthal, personal communication, 1930) Of 232 cases of atrial fibrillation due to thyrotoxicosis Hurxthal found that 38 per cent had also congestive failure. Thus atrial fibrillation may be considered to be but a stepping stone to congestive failure, an argument against such an actual entity as thyroid myocardial disease, since atrial fibrillation often occurs without evidence of disease in the heart muscle. In Ernstene s series of 1 000 cases of hyperthyroidism, 44 (4 4 per cent) *had congestive heart failure the two most important factors* responsible for this complication were organic heart disease and uncontrolled atrial fibrillation.

The systolic blood pressure is usually somewhat elevated in thyrotoxicosis,

averaging 140 to 150 mm mercury; in one quarter to one third of the cases it exceeds 150. The diastolic pressure is usually at a slightly decreased level averaging 60 to 70 mm. Thus, the pulse pressure is generally increased and the arterial pulse is full.

The roentgen ray study of the heart in thyrotoxicosis shows often considerable prominence of the pulmonary artery (probably secondary to the marked increase in the pulmonary circulation) and unusually energetic rapid heart action, these two signs are together very suggestive and almost pathognomonic of thyrotoxicosis, especially with the subject in the resting state. In spite of overactivity however the heart sometimes appears to be lacking in tone in the presence of thyrotoxicosis. Aortic regurgitation also gives markedly increased cardiac action, in a young person especially but the considerable cardiac enlargement and the aortic diastolic murmur make the differentiation easy; the water-hammer pulse is not so good a differentiating sign, for in occasional cases of thyrotoxicosis with much peripheral vasodilatation there is a well-marked Corrigan pulse. If cardiac enlargement is present it is best made out by roentgenologic study. Arrhythmias may be seen fluoroscopically but are not so well distinguished as by electrocardiography. Unusual clearness of the lung fields has been noted as occurring in thyrotoxicosis, probably largely because of the thin chest walls of most of the patients.

The electrocardiogram shows no specific effect of thyrotoxicosis. The tachycardia and arrhythmia that may be present are readily seen but the individual complexes are otherwise normal. It was thought years ago that the *T* wave might be found unusually high because in hypothyroidism the *T* wave is always low but this has proved not to be the case; in fact in many cases the *T* waves are low and in rare cases may actually be inverted in Lead 2 (Graybiel and White, 1935), doubtless a sympathetic nervous effect, it has been shown that sympathetic stimulation contrary to early ideas lowers or inverts the *T* waves, while vagus stimulation raises them (Hartwell, Burrett, Graybiel, and White, 1942).

The basal metabolic rate during the active stage of thyrotoxicosis is always high, though it varies considerably with the individual case being studied. A rate of 50 to 75 per cent above normal is not infrequent, 25 to 30 per cent above normal is considered to be on the borderline and demands close scrutiny for signs of thyrotoxicosis. It must be remembered that careful technic and avoidance of excitement are essential before judgment can be passed confidently on a borderline case or even on one that shows a distinctly high rate. Also it is important that repeated basal metabolic rate determinations should all show high readings in confirmation of the diagnosis of thyrotoxicosis; one or two readings in doubtful cases are inadequate. Congestive heart failure alone may definitely raise the basal metabolic rate to about +30 per cent, apparently as the result of increased work occasioned by the labored breathing; it has been reported as high as 40 to 50 per cent above normal, though such increase is unusual. The pulse rate, pulse pressure, and blood flow are all usually increased proportionally to the rise of the basal metabolic rate. Al-

though operative relief or spontaneous remission of active thyrotoxicosis may occasionally leave behind some cardiac involvement, especially atrial fibrillation, symptoms and signs usually subside along with the metabolic rate. It should be added that very rare cases of thyrotoxicosis may have basal metabolic rates within the normal range (0 to +10 per cent, for example) such patients probably represent the small group of individuals who normally show low rates (−20 to −30 per cent) without myxedema. Thus all evidence is necessary besides the basal metabolic rate, in difficult diagnostic cases.

Two more specific tests for thyrotoxicosis than the basal metabolic rate have been introduced in the past few years they consist of (1) the measurement of the protein bound iodine in the blood, which should normally not exceed 7.5 to 8 0 gamma per cent, and (2) the calculation of radioactive iodine (I 131) uptake by the thyroid gland which should normally not exceed 50 per cent but which in thyrotoxicosis is much increased. This latter test is much more accurate than either the former or the basal metabolic rate determination.

One of the most important of all diagnostic clues is the rapid and favorable response of true thyrotoxicosis to iodine therapy

Course and prognosis. The course and prognosis of thyrotoxic heart disease are extremely variable and depend on the severity and duration of the thyrotoxicosis. The abnormal condition of the heart may be scarcely noticeable and with the clearing up of the cause of trouble occasion no further symptoms and few or no signs. With very severe thyrotoxicosis that has lasted for a long time, heart disease may be evident by the presence of enlargement, atrial fibrillation and congestive failure, but there are infrequent exceptions when the heart may appear to be perfectly normal even after a good many years. The usual case of average "toxicity" shows in the course of years heart changes that are more than "functional" If there is no operative relief or spontaneous remission death from heart failure may ensue in such cases after a few more years. *Of a series of 178 fatal cases of thyrotoxicosis, 27 showed severe congestive failure, in 9 of which no other factor could be found than the thyrotoxicosis alone* (Kepler and Barnes, 1932) Other complications such as pneumonia may intervene to end the story Now and again in wasted and pigmented aged individuals, chronic heart disease can be traced back to a former thyrotoxic state but is very likely to be wrongly interpreted as "arteriosclerotic". If the thyrotoxicosis is still active in these cases operation or other specific therapy should be carried out and may be expected to afford considerable relief

It is to be noted that thyrotoxicosis tends to recur after subtotal thyroidectomy in about 10 per cent of the cases (Greene and Hurxthal, 1941) hence the return of atrial fibrillation or other signs or symptoms during the years following operation should make one think of this possibility

Complications. The commonest cardiac complication of thyrotoxicosis is atrial fibrillation which may occur at first as a functional disturbance alone

with little or no actual heart disease. In the late stages of thyrotoxic heart disease congestive failure may supervene. It is of much interest that in thyrotoxicosis, as in beriberi, the cardiac output may continue to be increased well above the normal despite the presence of considerable congestive heart failure with elevated systemic venous pressure.

Chronic rheumatic valvular disease is an occasional complication of thyrotoxicosis, and atrial fibrillation may lead to a diagnosis of one or the other condition when both are present. Coronary heart disease may be another complication, in the older cases, and the combination may produce angina pectoris. Hypertension of high grade may also occur (in about 10 per cent of the cases) the systolic blood pressure in thyrotoxicosis itself rarely exceeds 160 mm mercury

Treatment. The treatment of the heart condition resulting from thyrotoxicosis is fourfold (1) therapy of the thyrotoxicosis, (2) therapy of heart failure, (3) therapy of atrial fibrillation, and (4) observation for recurrence of abnormal thyroid activity

The first of these therapeutic procedures, namely the treatment of the thyrotoxicosis, comes foremost in the consideration of almost every case because not only does this therapy control the cause of trouble but it actually may relieve, without further therapy either or both of the serious complications, congestive failure and absolute arrhythmia.

After careful trial of other methods of treatment of active thyrotoxicosis (either ordinary exophthalmic goiter or adenomatous goiter) a good many authorities (e g., Means et al., personal communication, 1951) still believe that the best therapy in the present state of our knowledge is subtotal thyroidectomy Rest in bed and roentgen irradiation, though they have been apparently effective in some mild cases are far less dependable in the long run, and any delay of proper treatment may do harm.

A useful measure in the preparation of patients for operation has been the administration of iodine for one to two weeks for example, potassium iodide 5 gr (0.3 gm) once daily in saturated solution, the 5 minims or grains containing 330± mg of iodine, or Lugol's solution 10 minims (0 60 cc) containing 60 mg of iodine, three times a day for ten days. Iodine promotes the storage of thyroglobulin in the follicles and places a barrier in the way of escape of hormone from the gland (Lerman and Salter 1936) hence the high basal metabolic rate, the fast pulse rate and all the symptoms of thyrotoxicosis are much abated and the patient is a better risk for operation. Iodine therapy alone is not sufficient to control the thyrotoxicosis constantly except in a few mild cases. It has also been shown that thiouracil will control the basal metabolic rate prior to operation in the dosage of 300 mg of propyl thiouracil daily and divided into three doses given eight hours apart this is continued until there has been much improvement in the patient's condition at which time it is wise to give 5 to 10 drops of saturated solution of potassium iodide daily for ten days along with the thiouracil, ending with the surgical operation. Thi-

ouracil and related preparations have in some cases been used successfully in controlling thyrotoxicosis without operation, however toxic effects, especially on the blood, limit its use

Shortly after operation when the occasional stormy reaction has subsided it is usually discovered that the heart condition is much improved if not, and the thyrotoxicosis continues, further treatment may be necessary With careful preparation and the expert anesthesia and surgery that are essential for the best results, remarkable benefits have been frequently secured, even in cases which were apparently hopeless because of heart failure and which have been considered generally as poor operative risks. The relief of the thyrotoxicosis in such cases has proved far more important in the relief of the heart trouble than have remedies like digitalis and rest in bed directed to aid the heart condition alone. It is to be noted further that iodine has far more effect than digitalis in reducing the pulse rate in the tachycardia of thyrotoxicosis per se; in fact, digitalis is almost invariably ineffective in this respect while iodine is nearly always at first effective.

An ingenious therapeutic technic recently introduced for thyrotoxicosis consists of the use of irradiated iodine (I 131) orally adequate control of the disease has been effected without surgery a desirable achievement in cases where the cardiac status is precarious. Incidentally as will be noted in the chapters on "Coronary Heart Disease" (Chapter 21) and on "Congestive Heart Failure" (Chapter 30) irradiated iodine (I 131) has been used effectively by Blumgart, et al. (1948) to control both coronary and myocardial insufficiency through the production of a "medical thyroidectomy

The therapy of the heart failure due to thyrotoxicosis consists primarily as noted above, in the control of the thyrotoxicosis itself by the administration of iodine and operation, rest, digitalis, and diuretics are additional therapeutic measures, not very effective, however until the high metabolic rate has been reduced. The tolerance of thyrotoxic patients for digitalis is usually quite marked and the therapeutic dose of this drug must be proportionately increased, sometimes as much as 50 to 100 per cent above the ordinary dosage, in order to obtain any appreciable effect, whether beneficial or toxic, but only under careful observation.

The third therapeutic measure consists of treatment of the atrial fibrillation that may complicate thyrotoxicosis. There is little likelihood of control of this arrhythmia while thyrotoxicosis persists, but there is a fair chance, almost an even chance, that relief of the thyrotoxicosis alone will relieve also the atrial fibrillation. If it does not do so quinidine will restore normal rhythm in about half of the remaining postoperative cases in whom this arrhythmia persists, while digitalis can be used permanently to control the ventricular rate in the rest of the cases with persistent atrial fibrillation. The method of administering digitalis and quinidine will be discussed in Chapters 30 and 33 of this book. For paroxysms of atrial fibrillation either before or after thyroidectomy rations of quinidine sulfate (3 to 6 gr 0 18 to 0 36 gm three or four times daily) may be tried, they are more likely to be successful after operation.

Differential diagnosis. Thyrotoxicosis as a cause of cardiac enlargement, failure, and atrial fibrillation must be differentiated particularly from rheumatic heart disease and essential hypertension. Moreover when patients presenting obvious signs of rheumatic or hypertensive heart disease with congestive failure do not obtain relief from the usual therapeutic methods thyrotoxicosis should be suspected as a possible complication.

The early stage of thyrotoxicosis, before definite cardiac signs have developed, is especially to be distinguished from neurocirculatory asthenia. Its differentiation is not always a simple matter: it is sometimes impossible when the basal metabolic rate is at the normal borderline and there is no definite exophthalmos or thyroid gland enlargement—most of such cases prove later not to have any definite thyrotoxicosis. The differential diagnosis requires especial care if one has to deal with a patient who has both neurocirculatory asthenia and a colloid goiter

Rare atypical cases with overactive thyroid glands are found without exophthalmos or goiter: a slight staring anxious expression, unexplained loss of weight, diarrhea, pigmentation of the skin, and tachycardia may afford clues. When in doubt the basal metabolic rate should always be determined and repeated as often as necessary and especially the protein bound iodine in the blood should be determined (normal = 4 0 to 8 0 gamma per cent) or the radioactive iodine uptake (normal = 20 to 50 per cent at the end of 48 hours) Finally a therapeutic test with iodine may be carried out (Means, 1937)

HYPOTHYROIDISM. MYXEDEMA HEART

The state of underactivity of the thyroid gland, consisting typically of myxedema in adults and of cretinism in children, is an infrequent condition itself and a still rarer cause of appreciable heart disease. However in almost every case some abnormality of cardiac function is evident in the sluggish heart action and especially in the uniform flattening or inversion of all the *T* waves of the electrocardiogram (Figure 92A, page 454) these abnormalities are corrected by thyroid therapy (Figure 92B) Enlargement of the x-ray heart shadow sometimes at least due to pericardial effusion, is also a usual finding in severe myxedema, in some cases it is very striking, while in others, due to the wide range of the normal heart size, it may become evident only in the process of taking serial roentgenograms. It generally subsides under thyroid treatment with astonishing speed and degree (Figure 93 page 455) Arteriosclerosis likewise is frequent in myxedema.

The term "myxedema heart has been applied to a condition ound in about three quarters of the cases of myxedema (Zondek, 1918 1919 Fahr 1925 1927 1932 Fournier 1942) and this will be described below In many cases of myxedema, however especially the milder ones, it is difficult or impossible to make out any important abnormality of the heart caused directly by this glandular deficiency The cretin, too, has no very definite heart disease but

shows, as in myxedema, abnormal electrocardiographic *T* waves and sluggish cardiac action

Etiology Cause It is evidently the lack of sufficient thyroid secretion in myxedema which occasionally causes definite heart trouble in the form of enlargement or weakness or pericardial effusion, for the administration of rations of thyroid gland corrects this trouble. In what way the hypothyroidism causes this cardiac abnormality and what other factors may favor this effect, we do not know

Myxedema itself is usually of unknown origin but infrequently it follows thyroidectomy which is carried out to cure thyrotoxicosis. Myxedema was intentionally produced about 18 years ago in a new treatment of intractable angina pectoris and myocardial insufficiency by the surgical operation of total thyroidectomy (see Chapters 21 and 30) but this form of treatment was

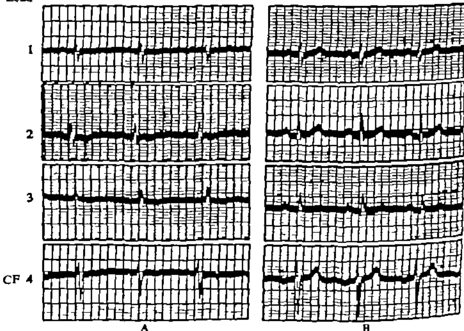


FIG. 92. Electrocardiograms (four leads) in hypothyroidism (myxedema) male, age 59 (*A*) before and (*B*) after thyroid therapy Basal metabolic rate at time of (*A*) = —46 per cent, and at time of (*B*) = —17 per cent.

found impracticable and given up. However there has been recently a revival of the principle of therapy involved, in the form of a medical thyroidectomy via irradiated iodine, with prevention of any high degree of hypothyroidism by the administration of small doses of thyroid

Age The myxedema heart, like myxedema itself has been found usually in middle age or later but it may occur in youth. It is likely that a complication such as coronary heart disease, coming independently or favored by the myxedema may help to account for the greater frequency of cardiac dilatation and weakness among the older victims of myxedema.





FIG. 93. Roentgenograms showing great change in cardiac area (6 cm in the transverse diameter of the heart shadow) as the result of the successful treatment of myxedema by thyroid administration. Woman, 66 years old.

(*A*) Dec. 5, 1934 basal metabolic rate = —46 per cent.

Cardiothoracic ratio in roentgenogram = $\frac{18.2}{34.0}$

(*B*) May 1 1935 basal metabolic rate = —13⅓ per cent.
In this record the diaphragm is somewhat lower than in the former which exaggerates slightly the difference in size of the heart shadow

Cardiothoracic ratio $\frac{12.2}{23.2}$

(Kindness of Dr J C. Gant, Madison College, Tennessee.)

Sex Sex has no particular relationship to the myxedema heart so far as we know

Other factors The most important factors controlling the incidence of the myxedema heart in any community are undoubtedly first, the frequency of myxedema itself in that community and, second, the ability of the medical profession to recognize and properly to treat it. It undoubtedly is a preventable type of heart disease.

Pathology An occasional finding in myxedema is considerable globular enlargement of the x ray heart shadow giving rise to the so-called myxedema heart. The exact cause of such enlargement is not always clear and has been a subject of some controversy· probably it is the result partly of dilatation, partly perhaps of the increased bulk due to the myxedematous state affecting the heart tissues, and certainly sometimes to an excess of fluid in the pericardium, all three factors may play a role in increasing the area of percussion dullness or the roentgen ray heart shadow Functional regurgitation through the atrioventricular valves may occur with the dilatation but there is no endocarditis. *Pericarditis is not found despite the occasional discovery of large pericardial effusions* the heart itself may show no actual enlargement in the midst of a large pericardial effusion. Presenile arteriosclerosis, especially involving the coronaries, is reputed to be a general accompaniment of myxedema, but convincing evidence of this is still lacking.

Symptoms. There are few symptoms of the heart involvement in myxedema, the low level of activity in this condition probably preventing the cardiac dilatation and weakness from making themselves more evident. Dyspnea has been noted in rare cases of congestive failure in myxedema and in a few patients with myxedema angina pectoris has occurred. These symptoms, occurring at the height of the endocrinopathy itself are sometimes cleared by thyroid therapy but sometimes induced or aggravated by the specific treatment which raises the metabolism and blood flow too rapidly coronary disease or other factors preventing the heart itself from keeping pace with the demands thus newly thrown upon it.

Signs. The only cardiovascular signs in the case of the myxedema heart are the occasional enlargement evident both on physical examination and by roentgen ray study (Figure 94) the sluggish heart action commonly observed in the same way and the constant finding of absence or inversion of the *T* wave in all leads of the electrocardiogram (Figure 93) This electrocardiographic sign is almost pathognomonic of myxedema and can be used along with the determination of the basal metabolic rate in following the progress of thyroid therapy There is frequently also a decrease in amplitude (low voltage) of the other complexes of the electrocardiogram the *P* and *QRS* waves, which resume along with the *T* waves a more normal extent of excursion on treatment.

The usual signs and symptoms of myxedema are generally obvious—slowed mental state, dryness and thickening of hair and skin, puffiness of subcutaneous tissue (myxedema) all over the body including the face, weakness, and dislike of cold. The basal metabolic rate is generally reduced to 30 per cent below

the average normal or lower borderline cases with measurements of basal metabolic rate of minus 10 to minus 25 per cent are less likely to have heart trouble, and usually these individuals have not true myxedema to start with.

Also in myxedema a decrease has been found in the cardiac output, circulatory velocity peripheral flow and total volume of blood.

Course and prognosis. The finding of evidence of significant cardiac involvement in myxedema is an important sign, for it means that the grade of myxedema is a serious one or that other heart trouble, such as coronary or hypertensive, is present. The discovery of cardiac enlargement is usually an incidental one in the course of routine examination but it should always be looked for and the cardiac response to the treatment of myxedema should be carefully followed. Sudden death with or without angina pectoris may occur a few months or years after the finding of the myxedema heart. Death postponed by careful thyroid therapy may come eventually from other complications without cardiac responsibility in fact a full length of life is possible under careful treatment. Congestive failure as a cause of death in myxedema per se is very rare; I myself have never seen a case.

Complications. Angina pectoris due to coronary disease is the most important complication of the myxedema heart, especially after treatment of the myxedema has begun, the elevation of metabolism by thyroid therapy may induce symptoms of coronary insufficiency Acute infections, like pneumonia, may appear as complications with serious prognosis. General arteriosclerosis is common but not essential.

Treatment. Digitalis has no definite beneficial influence on the cardiac enlargement or electrocardiographic abnormalities of myxedema. Thyroid gland, on the other hand, has a striking effect, clearing up these conditions more or less completely if given in sufficient dosage. An amazing decrease in heart or pericardial size may sometimes be effected, in four cases of Lerman, Clark, and Means series (1933) for example, the transverse diameter of the heart shadow by teleroentgenogram decreased in the first case from 19 3 to 12.4 cm in six months, in the second from 21 4 to 15 7 cm in six weeks, in the third from 16.5 to 11 4 cm in eight and one-half months, and in the fourth from 19 4 to 15.5 cm in five months.

Thyroid gland should be given very cautiously in the treatment of myxedema, particularly when there is a history of angina pectoris, for although marked general improvement may ensue and the heart resume practically normal size, angina pectoris may be precipitated or increased by the raised level of metabolic rate and increased blood flow and sudden death may occur just when the myxedema itself is under control. It may be necessary to give doses of thyroid so small that, although the basal metabolic rate is not restored completely to normal, angina pectoris is kept away or under partial control some myxedematous signs and symptoms may remain but life is prolonged. A dose of ¼ to ½ gr (0 015 to 0.03 gm) of thyroid (U.S.P) daily may accomplish this instead of the usual larger doses (1 to 2 gr) Rarely the thyroid therapy banishes angina pectoris. Digitalis should be given if there are, in addition to the dilatation of the heart, signs and symptoms of congestive failure

which do not yield to thyroid therapy alone, but morphine is contraindicated.

Differential diagnosis. The myxedema heart must be differentiated from cardiac enlargement and weakness of other cause, from coronary heart disease and from infectious pericardial effusion This is usually readily done by the absence of cardiac symptoms, of chronic valvular disease, and of hypertension, by the typical electrocardiographic findings, by the general signs of myxedema, and by the response to thyroid therapy

DISEASES OF OTHER GLANDS

Parathyroid disease. Little is to be said of the effect of parathyroid disease on the heart. The decreased calcium content of the blood in tetany is associated with increase of the duration of cardiac systole hyperparathyroidism and the administration of excessive amounts of parathormone cause by the increase of calcium content of blood, an increase of calcium in the tissues likewise, including the heart muscle. We have no proof that these results are of any clinical significance.

Pituitary disease. The only association of abnormality of the heart with pituitary disease is the finding of cardiac enlargement (hypertrophy) especially of the left ventricle in acromegaly such enlargement may be great and out of proportion to the general splanchnomegaly found in this condition. Whether it is the result of the somewhat increased basal metabolic rate in this disease or due to other factors is not known. In one series of 24 patients marked heart failure was noted in 18 (75 per cent) six of this group died from that cause (Mason, 1936 1938) In gigantism the heart is not affected but bears a normal relationship to body size (Zondek, 1920)

Basophilia of the posterior lobe of the pituitary gland has been noted in certain cases of pituitary adenoma with hypertension and in some patients with hyperplesia and eclampsia (Cushing, 1934) this finding has not been confirmed, however as a characteristic occurrence in essential hypertension.

Adrenal disease. Adrenal disease has a direct effect on the heart, as well as on the circulation. Destruction of adrenal tissue (cortex) as in Addison's disease, causes collapse, marked hypotension, and general muscular weakness, including myocardial weakness but not structural heart disease. The heart is smaller than normal both in volume and weight, in part the result of the decreased amount of circulating blood and in part due to myocardial atrophy and the *T* waves of the electrocardiogram are depressed.

Relief of the symptoms and signs of Addison's disease has been effected by adrenal plus sodium chloride therapy but the new specific therapy of adrenal insufficiency (Addison's disease) with desoxycorticosterone and cortisone must be followed with great care since serious cardiac enlargement and weakness may appear with toxic doses In fact measurement of heart size has been suggested as an objective check on large dosage of the hormone (McGavack, 1942) It has been found that "the dose of desoxycorticosterone acetate necessary to produce a given degree of cardiac enlargement varies inversely as the amount of sodium available in the tissues."

Not only may dilatation of the heart result from excessive desoxycorticosterone therapy of Addison's disease but even high degrees of congestive failure, along with changes in the electrocardiogram which recede or disappear when the drug is omitted. The tendency to low voltage of the *QRS* and *T* waves found with Addison's disease is much exaggerated by excess of desoxycorticosterone (Currens and White, 1944) These changes in the heart are probably due to, or at least associated with, a loss of body potassium. Illustrations of the changes in the electrocardiogram and roentgen picture of the heart due to excessive desoxycorticosterone therapy are shown in Figure 94 on page 460

The stimulation that results from an adrenal medullary tumor (*pheochromocytoma*) can cause hypertension of paroxysmal nature, which may be cured by removal of the tumor If the hypertension is sustained, however removal of the tumor may have no effect on it, splanchnic resection then being required. The tumor may be located in tissue outside the adrenal glands themselves and then may be found with difficulty

Cortical adenomas of the adrenal may also play a role in hypertension, they are more numerous than pheochromocytomas but their removal may not have any important effect on the hypertension present in such a case (Smithwick, personal communication, 1942)

Pancreatic disease. *Diabetes mellitus* does not cause heart disease directly but it does favor arteriosclerosis and coronary artery disease (Root, Bland, Gordon, and White, 1939) At least 50 per cent of all diabetics die as a result of cardiovascular complications and the relative incidence of this cause of death is steadily increasing as other fatal complications are eliminated. Marked atherosclerosis of the aorta with considerable dilatation is common. Hypertension plays an important role in this group and frequently precedes the onset of the diabetes, sometimes by several years. Congestive failure due to hypertension or to coronary disease is not unusual but death comes most frequently from coronary occlusion (West, 1935)

Excess of insulin does not apparently affect the heart seriously unless there is already heart disease the possible harmful effect from insulin shock (*hyperinsulinemia*) however makes it advisable to use insulin cautiously in the presence of acute coronary thrombosis, very severe angina pectoris, and congestive failure. Arrhythmias and electrocardiographic abnormalities following the use of insulin occur.

Thymic disease. Hypertrophy or persistence of the thymus gland is not attended by heart disease, but is accompanied by general arterial hypoplasia. The cause of the sudden death in the so-called status lymphaticus and its reputed relationship to the thymus gland are still unsolved mysteries. The enlarged gland in child or adult is to be differentiated on physical examination and by roentgen ray from abnormalities of the great vessels.

Genital glands. Heart disease does not result from disease of ovaries or testes, but functional disorders with cardiovascular symptoms of neurocirculatory asthenic type are commonly found, especially at the time of the menopause in women or following double oöphorectomy Hypertension of the essential type is also a frequent finding, often but temporary at the time of

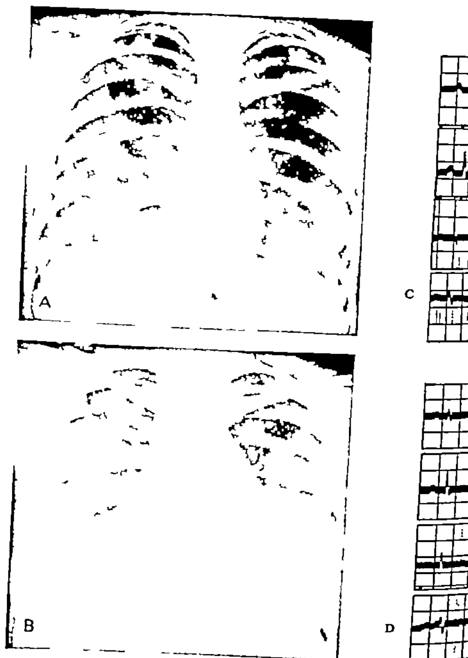


FIG. 94 Roentgenograms and electrocardiograms in the case of a young woman with Addison disease showing the toxic effect of excessive desoxycorticosterone acetate in treatment. (*A*) Roentgenogram of the thorax Aug. 13 194–, showing normal heart size and some prominence of the shadow of the pulmonary artery. (*B*) Roentgenogram of the thorax Sept. 9 1942, showing marked enlargement of the heart during the height of the effects from the desoxycorticosterone. (*C*) Electrocardiogram, more or less normal, of this patient on Oct. 4 194–, after the effects of the desoxycorticosterone had worn off. (*D*) Electrocardiogram on Aug. 30, 194–, at the height of the toxic effect of the desoxycorticosterone.

the menopause and thus may affect the heart secondarily to cause hypertrophy. Hamilton (1940) has not found, however, that the climacteric exerts any very severe strain on the heart of women already affected by heart disease. A so-called "fibroid" heart has been said to result from uterine fibroid disease (fibroma) but there is no proof that such a condition exists, functional disturbances as noted above and premature beats undoubtedly accounting for this condition. There has as yet been demonstrated no real "myoma heart" (von Jaschke, 1933). A change in the electrocardiogram consisting of a digitalis-like depression of the *ST* segments and *T* waves, was noted by Scherf (1940) in some females with ovarian dysfunction, and was cleared by estrogenic hormone therapy; such changes are, however, rarely more than slight in degree and it is probable that some factor such as hyperventilation (see Chapter 9) secondary to the climacteric rather than the ovarian dysfunction itself, is responsible.

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CHAPTER 19

HYPERTENSIVE HEART DISEASE
ESSENTIAL HYPERTENSION
HYPOTENSION

HYPERTENSIVE HEART DISEASE

Introduction. Since the last revision of this book seven years ago there have been innumerable studies and published reports concerning hypertension and hypertensive cardiovascular disease, many of them of considerable interest and value, as may be observed on perusal of the additions of references to representative publications in the Bibliography at the end of the chapter. Nevertheless the mechanism of the so-called essential type of hypertension still eludes us another few years may very well reveal to us the answer or the answers, since so many able workers are engaged on the problem. Meanwhile to date distinct advances in therapy though empirical, have been scored.

The most common and important of all types of heart disease by and large the world over is that due to systemic hypertension with elevation of the *diastolic* blood pressure. It is often serious and frequently followed by congestive failure and death. It has been estimated that nearly 100,000 people die annually in the United States (population of about 130 000,000) as the result of heart failure due to hypertension, and that 7 000 more die from other consequences of high blood pressure. In a series of 30,265 autopsies with 4 678 cardiovascular deaths (15 45 per cent) 2,597 were hypertensive cases (55.5 per cent of the cardiovascular deaths and 8 6 per cent of the total autopsies) the chief factor responsible for the hypertensive deaths was cardiac (2,059 cases or 79 per cent, divided into the group with myocardial insufficiency—congestive heart failure—with 1 124 cases or 43 per cent and that with coronary fatalities with 935 cases or 36 per cent) while cerebral hemorrhage caused death in 362 patients (14 per cent) and renal insufficiency in 176 cases (7 per cent) (Clawson 1941) In New England systemic hypertension is a primary or a secondary factor in at least 30 per cent of cases of heart disease. Until the last decade or two the condition had a variety of other names, or was missed entirely unless blood pressure studies revealed the hypertension. It has made up a considerable percentage of cases of so-called "cardiorenal disease," of so-called "myocarditis," and of cardiac enlargement or failure without valvular disease and of unknown cause.

Heart disease due to pulmonary hypertension is much less common than that due to systemic hypertension, but it is of considerable interest and importance, and will be discussed in the next chapter Hypertension in the portal circulation will be taken up in connection with diseases of the blood vessels in Chapter 28 Venous hypertension is discussed in Chapter 6 under Venous Blood Pressure and in Chapter 30 on Congestive Heart Failure.

Etiology Cause The cause of the heart disease is known—high blood pressure often abetted by some other factor especially coronary disease. The fundamental cause of the high blood pressure in the majority of cases has been, however obscure and not associated with any constant clinical findings hence, it has been called essential" or primary The term "hyperpiesia" (ὑπέρ, over and πιέζειν to press) has also been applied to it, and another synonym is vascular" or arterial hypertension," indicating that the blood vessels are responsible.

Innumerable theories as to the cause of hypertension have been advanced since its discovery over a generation ago and some of these theories have now become facts in other words, there are at least several different causes, although that of the bulk of the cases (those with essential hypertension) is still (1951) to be elucidated. The association of heart disease with kidney disease was demonstrated by Bright more than a century ago (1836) but the mechanism of such association was of course unknown. Gull and Sutton (1872) pointed out the arteriolar fibrosis found in Bright's disease, and in our own generation the vascular factor in hypertension has had the limelight. During the last decades, however attention has been directed again to the kidneys by the pioneer work of Goldblatt (1934) who demonstrated that hypertension can be produced in animals by obstructing by a clamp the blood flow through a renal artery and by the finding of pressor substances, called angiotonin and hypertensin, produced by the kidney with their neutralization by other (antipressor) substances (Tigerstedt and Bergmann, 1898 Houssay Fasciolo and Taquini, 1938 Page and his associates, 1940, 1941 Harrison Grollman, and Williams, 1940) Suffice it to say that the most acceptable and widely held theory in the light of our present knowledge is that the arterioles more or less universally throughout the body have through some direct toxic or nervous influence become irritable and pass into a state of vasoconstriction, thereby increasing the resistance to the circulation of blood, to which the heart responds with a resulting rise of arterial blood pressure. It is possible that the renal arterioles may play the major role in this process. At first this type of hypertension is slight and transient and may largely escape notice. Its later course is very variable the *arteriolar spasm* may subside with a spontaneous cure of the hypertension, it may increase and become fixed as in the ordinary well-recognized case or it may progress to an extreme and rapid degree giving rise to the so-called malignant hypertension. According to this theory there are at first *no* (as yet) recognizable pathologic changes arteriolar sclerosis, arterial sclerosis, renal damage (arteriosclerotic nephritis) and cardiac enlargement are secondary effects of long-sustained hyperpiesia in

time the *arteriolar sclerosis itself* may be responsible for at least some of the hypertension and prevent its reduction.

Hypertension is in some cases (a distinct minority) secondary to an easily discoverable cause, such as gross nephritis, polycystic kidneys, adrenal tumor increased intracranial pressure or congenital coarctation of the aorta, or is temporarily induced by urinary obstruction, congestive heart failure coronary insufficiency pain, exertion, or excitement, or concussion of the brain frequently slight systolic hypertension attends thyrotoxicosis, complete heart block, and aortic regurgitation or marked sclerosis. Under such circumstances the hypertension is not called essential or hyperpiesia. In the case of hyper tension of renal origin there may be an added toxic effect from renal insufficiency with or without definite uremia. The "surgical kidney" as such is not, however commonly a cause of hypertension.

A number of practical classifications of hypertension have been proposed in the past, a good example of which, presented by Gilchrist (1941) was published in the third edition of this book. A recent system, bringing this subject up to date, has been presented by Page (1949) This is reproduced below It is to be observed that diastolic hypertension is far more important than systolic hypertension systolic hypertension with normal or only very slightly elevated diastolic blood pressure is much less important clinically and is apparently in the main the result of arteriosclerosis.

Table 8

CLASSIFICATION OF HYPERTENSION (PAGE)

Clinical	*Experimental*
I. Nervous Participation	
Poliomyelitis of brain stem	Cerebral ischemia
Porphyria	Cushing's experiment
Increased intracranial pressure	Resection of sinus and aortic depressor nerves
Sclerosis of carotid sinus	
Resection of glossopharyngeal nerve	Hypertension from audiogenic stimulus
Emotion	
Tabes dorsalis	
II. Cardiovascular Participation	
Coarctation of aorta	Clamping of aorta above renal vessels
Heart failure	
Arteriovenous fistula	
Arteriosclerosis	
III. Endocrine Participation	
Hypophysis—basophil adenoma	Anterior lobectomy diminishing blood pressure
Adrenals—pheochromocytoma	
Cortical carcinoma	Adrenaline hypertension
Cortical hyperplasia	Desoxycorticosterone acetate hypertension
Thymus—carcinoma with Cushing's syndrome	Bilateral adrenalectomy abolishes hypertension
Placenta—associated with toxemia of pregnancy	Cerebrum (1951)

IV Renal Participation

Glomerulonephritis	Antikidney serum nephritis
Obstruction to renal vessels	Mechanical constriction of renal arteries or veins
Pyelonephritis	Mechanical compression of ureters
Prostatic obstruction	Cellophane or silk perinephritis
Polycystic kidneys	
Crush syndrome	
Periarteritis nodosa	
Perinephric constriction of the parenchyma	

Hyperpiesia (essential hypertension) accounts for fully 95 per cent of the cases of hypertensive heart disease, and obvious renal disease for most of the rest. About two thirds of the cases of established diastolic hypertension show cardiac enlargement on examination. Still others have lesser grades of enlargement too slight to discover clinically hypertension, whether or not of the essential type, may be too slight or recent in onset to cause any cardiac hypertrophy at all.

Age Hypertensive heart disease, like hypertension itself (especially hyperpiesia) is commonest in middle age and after signs of it appear on the average ten years after the onset of sustained hypertension of an important degree except when there are complications (valvular disease or coronary disease) to make its effect more quickly evident. Of a series of 708 cases of hypertensive heart disease 62 per cent were in the sixth and seventh decades (29 per cent in the sixth and 33 per cent in the seventh) 17 per cent were over seventy years of age, 16 per cent were in the fifth decade, 4 per cent in the fourth, 1 per cent in the third, and 0.5 per cent were below twenty years old, thus only 21 per cent of the cases were less than fifty years of age (White and Jones, 1928) In a more recent series of 1,249 cases 68 per cent were between fifty and seventy (White, 1936) The youngest case of essential hypertension with autopsy on record that I know about has been reported by Taussig and Remsen (1935) a colored boy two years old.

Sex. There is not much difference between the sexes in the incidence of hypertensive heart disease. In White and Jones series of 708 cases 55 per cent were female and 45 per cent male. In the more recent series of 1,249 cases from my own practice, 51 per cent were male and 49 per cent female. Hypertension itself on the other hand, is far more common in females than in males, by a ratio of about 2 to 1 Yet it is true that it is much more serious in the male Blackford and Wilkinson (1932) found the mortality rate after ten years twice greater in men and among 50 consecutive cases of my own with serious cardiovascular sequelae of hypertension selected for sympathectomy 38 were male and 12 were female (White et al., 1950)

Heredity Of all known etiologic factors in the production of hypertension, and so of hypertensive heart disease, heredity ranks as of the greatest importance. Frequently many members of one family in the course of a few

generations have either shown essential hypertension or have had troubles coming from such a condition. The way in which heredity acts is obscure but we do know of its great significance.

Race and *climate* are factors of some importance. Hypertension is less marked in tropical and semitropical climates and it is said to be uncommon in certain nationalities like the Chinese when in their own country whether this is because of race or of other factors like tempo of life or diet we do not know It is especially common among the Negroes in the United States, apparently twice as common as in the white population, for reasons unknown it is said that in Africa on the other hand, hypertension is rare among the Negroes who tend, however to succumb to other ills, especially tropical diseases, at relatively early ages, before the years when essential hypertension is at its peak in America. We need much international research on this problem.

Diet and obesity Overeating and obesity frequently are associated with hypertension and hypertensive heart disease, but the relationship is a very inconstant one on both sides. A high protein diet was once blamed for the production of hypertension, but this has been refuted on the other hand, a diet overrich in food value in general may be of importance. During the war in Holland over a period of starvation from September 1944 to May 1945 there was a frequent lowering of blood pressure, associated with weight loss, especially in hypertensive patients (Lups and Francke, 1947) There are problems here in need of solution.

Nervous and physical strain. It is believed by many observers that a life of high nervous tension favors the production of hyperpiesia or at least its aggravation the latter is the more likely Physical strain and constant laborious work, although sometimes blamed as aggravating factors, have been largely exonerated in late years indeed it seems possible that physical exercise, in moderation at least, may protect against hyperpiesia.

Endocrine disturbances are frequently attended by hypertension but rarely by marked hypertension these disturbances are especially associated with the ovarian function (for example, menopause and oöphorectomy) with thyrotoxicosis, and with adrenal or pituitary tumors. In the case of thyroid or adrenal or pituitary oversecretion surgical removal of a large part of the thyroid gland or of an adrenal or pituitary tumor may result in a return of blood pressure to normal. The discovery that an excess of basophilic cells is present in the posterior lobe of the pituitary gland (hypophysis) in certain cases of pituitary adenoma with hypertension and of eclampsia (Cushing, 1932) suggested that hyperplesia might have its basis therein but this suggestion has not been confirmed, only a small minority of cases are to be so explained.

Infections and poisons have not been shown to have any close connection with the pathogenesis of hyperpiesia this statement includes lead, long blamed for hypertension.

Pathology The pathology of hypertensive heart disease is as a rule very

simple. Both cardiac and vascular abnormalities in chronic hypertension are primarily but natural responses of muscle to increased work. Hypertrophy of the individual muscle fibers of the left ventricle is always present, sometimes to such a degree that the heart is greatly enlarged (Figure 95) A heart weight of about 500 gm (normal = 200 to 350 gm) is common and in rare cases this may be increased to 750 or even to 1 000 gm. With the development of failure

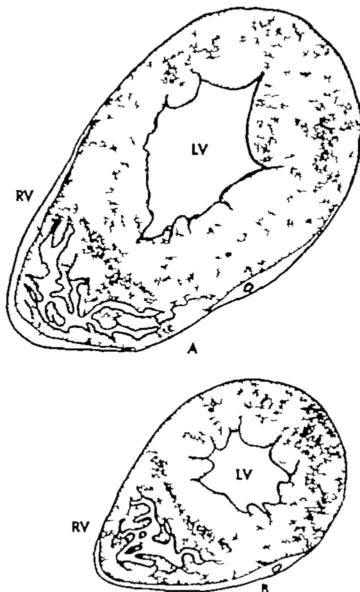


FIG. 95 Drawings showing cross sections (actual size) of (*A*) an enlarged hypertensive heart, and of (*B*) normal heart at level two thirds of the distance from base to apex of the ventricles. LV = left ventricle, RV = right ventricle.

dilatation appears, changing the appearance of left ventricular hypertrophy from "concentric" to "eccentric." Such left ventricular dilatation is followed by dilatation of the mitral valve ring, functional mitral regurgitation, dilatation of the left atrium and enlargement of the right ventricle and atrium too, if the left ventricular failure lasts long enough. It has been suggested that the "primary" hypertrophy of the heart muscle begins only after it has been strained or traumatized and somewhat dilated by the early efforts to overcome the effect of the arteriolar constriction. Since with systemic hypertension the pulmonary arterial blood pressure usually remains normal (until the left ventricle fails) the right ventricle is unaffected early in the disease. Eventually after the left ventricle has begun to fail the pulmonary blood pressure rises and the right ventricle in its turn is subjected to considerable strain and begins to enlarge as a matter of fact the commonest cause of right ventricular enlargement is failure of the left ventricle secondary to systemic hypertension.

There is no actual myocarditis or myocardial degeneration in most cases of uncomplicated hypertensive heart disease, even in massive hearts with marked congestive failure some myocardial scarring (fibrosis usually in small areas) is, however not uncommon, even in the absence of coronary disease (Levine, V 1934) Endocarditis and pericarditis do not occur primarily in this type of heart disease, although endocardial sclerosis, most marked in the left atrium which first bears the brunt of left ventricular failure, was found in all of a series of 27 hypertensive hearts (Levine, V., 1934)

The aorta, normal at first, becomes dilated in older and chronic cases, but never to the degree observed in advanced syphilitic aortitis. Some of the dilatation seen by roentgen ray examination is not found post mortem, since it is temporary depending on the intra-aortic hydrodynamic state. The vascular dilatation may extend a little into the aortic branches, especially into the innominate and carotid arteries. Rarely the aortic media may split to cause a dissecting aneurysm when hypertension is complicated by an abnormally weak spot in the aortic wall.

Thickening of the arteries and arterioles throughout the body is a common finding in chronic hypertension and in all probability is a vascular response to the hypertension Arteriolar sclerosis and obliteration may complicate the picture. Hypertension without arteriosclerosis and arteriosclerosis without hypertension are frequent findings, but the two combined are as frequent as either condition alone Renal arteriolar sclerosis is preponderant, and is universally found in the higher grades of hypertension, although not as a rule at the onset of the disease.

Symptoms. There are no symptoms of hypertensive heart disease until complications arise· the condition is often discovered incidentally in the course of routine examination. *Usually the person feels perfectly well* and is simply annoyed by the discovery of the high blood pressure or of the enlargement of the heart. Occasionally however there are headaches and a coincident neurocirculatory asthenia with its various symptoms including palpitation, heartache, and dyspnea. These symptoms are frequently erroneously attributed

by patient and doctor alike either to the high blood pressure or to heart disease, although it is true that a person subject to neurocirculatory asthenia will have more symptoms if the blood pressure is high and the heart is enlarged than when the blood pressure and heart are normal, and in some cases headache is part of a disturbance of the cerebral circulation incident to the hypertension ("hypertensive encephalopathy") A neurosis is common with hypertension and hypertensive heart disease, usually the result of fear of the high blood pressure. When true symptoms of hypertensive heart disease do arise they are most commonly those of cardiac insufficiency which may increase to well-marked congestive failure, resulting from the myocardial strain and fatigue which involve primarily the left ventricle.

Dyspnea on exertion is usually the first authentic symptom, tending to increase in degree unless checked by the institution of proper treatment. With marked failure dyspnea may become constant and prevent a recumbent position (orthopnea) Or there may be sudden attacks of acute failure of the left ventricle occurring during sleep at night or less often in the daytime after exertion or excitement, with engorgement of the pulmonary circulation, pulmonary edema, and sometimes the setting off of asthmatic respiration. Such an attack of wheezing is called cardiac asthma and is not an infrequent syndrome in the case of the failing hypertensive heart It varies considerably in duration but lasts usually about an hour

Pain is less common in hypertensive heart disease than is dyspnea. It takes two forms, sometimes a precordial ache due to an associated neurocirculatory asthenia (or effort syndrome) aggravated by the cardiac enlargement, and sometimes angina pectoris, from an associated coronary disease or syphilitic aortitis. Angina pectoris, however though common in hypertension because of the age incidence, is not so characteristic as is dyspnea, for the hypertensive strain results in an inability of the left ventricle to maintain the general circulation more often than in the inability of the coronary circulation to supply the heart muscle with blood, unless we accept the possible theory that some hypertension, especially if it involves the diastolic pressure, may result from the need of greater force to maintain an adequate coronary circulation. The prolonged pain of coronary occlusion occasionally complicates hypertensive heart disease.

Palpitation is common in hypertension with or without heart disease, especially in sensitive persons, due either to the consciousness of the forceful heart action with normal rhythm, particularly on exertion or excitement, or to the occurrence of unimportant premature beats, paroxysms of tachycardia, or atrial fibrillation. These various disturbances of rhythm are common in hypertensive heart disease but they are not characteristic. Of the group of 708 cases of hypertensive heart disease of White and Jones (1928) 92 (or 13 per cent) had atrial fibrillation (14 of these were paroxysmal in type) paroxysmal tachycardia was noted in 11 patients (1.5 per cent) atrial flutter in 2 (0.3 per cent) and atrioventricular block in 13 (1 8 per cent)—the last named being due to an associated coronary disease and not to the hypertension.

Other symptoms frequently found in essential or in nephritic hypertension with or without heart disease are familiar: tinnitus, weakness, nosebleeds or other hemorrhages, symptoms of cerebral accident (aphasia and paralysis) whether transient (hypertensive cerebral vascular crises or minute lesions) or more or less lasting (cerebral hemorrhage or thrombosis) and symptoms of renal insufficiency (drowsiness, coma, and vomiting from uremia). The term hypertensive encephalopathy is used to cover all the various cerebral vascular disturbances due to hypertension from slight dizziness to extensive apoplexy. In frequency as a serious complication it ranks below the cardiac effects but above the renal.

Signs. The only constant sign of hypertensive heart disease is cardiac enlargement, due mainly to left ventricular hypertrophy. The hypertension itself responsible for this enlargement may have subsided at the time of examination, though some trace of it usually exists. If there is no increase in heart size even though hypertension is present we cannot label the condition hypertensive heart disease, although, as after rheumatic fever, we may speak of potential heart disease. *In the early stages of hyperpiesia and even in more chronic* cases when the blood pressure is but slightly elevated, the heart may be able to stand the strain without increase in size, but a normal heart size is rare, if it exists at all, with markedly high blood pressure of long duration. Finally it is to be observed that the cardiac enlargement of hypertensive heart disease may be present in slight degree, to be discovered only at postmortem examination, not being sufficient to give evidence during life. An addition to the heart weight of 25–50 or perhaps even 100 gm, in the absence of dilatation, can probably not be detected clinically even by careful roentgen ray examination unless there are frequent serial records. Hence the clinical statistical report that about two thirds of the cases with hypertension eventually show cardiac enlargement undoubtedly falls somewhat short of the actual figure as indicated by the statistical study of Murphy and his associates (1932) who found that in a series of 375 cases of essential (primary) hypertension examined post mortem the heart weights were 400 gm or above in 81.87 per cent (*normal upper limit of heart weight = 350 gm in the male and 300 gm in the female*).

In systemic hypertension with or without heart disease the aortic second heart sound is usually accentuated, sometimes to a striking degree. When the left ventricle begins to fail the pulmonary second heart sound increases in intensity in its turn as the pulmonary blood pressure rises, and finally the pulmonary second sound equals or quite commonly exceeds the aortic second sound in intensity even though the latter continues to be louder than normal. The changing relationships of the intensities of these two sounds is of great interest and importance, affording a valuable but much neglected clue to the degree of sufficiency of the left ventricle.

With increasing size of heart and the development of dilatation of left ventricle and aorta under the strain of the hypertension, apical and aortic systolic murmurs appear and are common in the more advanced cases, the former due to functional mitral insufficiency and the latter chiefly to the aortic dilata-

tion. In still more advanced cases, especially when arteriosclerosis complicates the picture, the aortic valve ring itself may stretch, either temporarily under the head of pressure or more or less permanently to give rise to an aortic diastolic murmur (aortic regurgitation, usually "functional"). In a series of 300 cases of hypertension (Paullin, 1927) a mitral systolic murmur was noted in 26 per cent, an aortic systolic murmur in 6 per cent, and an aortic diastolic murmur in 2½ per cent. In another series of 200 consecutive autopsied cases of hypertensive heart disease with normal aortic valves, reported by Garvin (1940) a diastolic murmur had been heard at the base of the heart, apparently aortic in origin, in 14 cases, resulting in a frank error in etiologic diagnosis in four instances.

The aortic dilatation due to hypertension may not be marked enough to be found on physical examination but it is generally easily seen fluoroscopically. It consists of a general enlargement of the whole thoracic aorta. The ascending aorta is not, as a rule, so dilated as in syphilitic aortitis, and there are no aneurysmal pouches. A point of especial interest concerning the aortic dilatation in hypertension and incidentally also in cases of aortic regurgitation is that the dilatation is at first "functional" or dynamic, at that stage failing to appear at autopsy even though very evident by roentgen ray examination during life.

A common sign, resulting from two factors, the vascular dilatation and the pushing up of the great vessels by the cardiac enlargement and the high diaphragm so often found in obese persons, especially women, with hypertension, is a prominence with pulsation of the innominate artery and the origin of the carotid artery at the base of the right side of the neck just above the inner end of the clavicle; this is so marked sometimes that it resembles a small aneurysm.

When congestive heart failure, arrhythmias or other complications arise the usual signs of such troubles appear and the heart tends in the case of failure to become very large with increasing dilatation. The appearance of gallop rhythm of the protodiastolic type is a frequent and serious sign of cardiac dilatation and failure in hypertensive heart disease. The relative frequency of arrhythmias in hypertensive heart disease has been noted above; their incidence is less in hypertension as a whole. One of the most important disorders of heart action—pulsus alternans (see Chapter 8)—is relatively common in the case of the failing hypertensive heart and is much more common than generally thought; it is most readily detected during the course of blood pressure measurement and it usually means that death is at best but a few years off (see Chapter 30).

One of the most helpful and constant signs of chronic hypertension, and therefore usually associated with hypertensive heart disease, is sclerosis of the arteries in the eye grounds (fundi oculorum); this is far more constant than in the case of general or coronary arteriosclerosis or of nephritis. In slight to moderate grades of hypertension there may be little change in the fundi, from none at all to "silver wire" appearance of the arterioles with nicking of the veins where the arteries cross them, but in advanced or serious cases

hemorrhages appear in the eye grounds and areas of degeneration are found (see Figure 9 page 54) Moreover an early finding of marked retinal changes suggests that the type of hypertension is "malignant" with a bad prognosis (even though the kidneys may be relatively normal at the time)

Signs of serious involvement of the brain may appear in the course of hypertensive heart disease, such as paralyses and abnormal reflexes, or there may develop evidence of involvement of the kidneys albuminuria, many casts in the urinary sediment, oliguria low specific gravity of urine, lowered renal function, and nitrogen retention in the blood, but it is to be remembered that in congestive heart failure due to hypertension, albuminuria, casts, and other urinary abnormalities may be caused by congestion without nephritis, and that a relatively unimportant vascular nephritis may develop secondarily due to the hypertension, with such signs as those noted above and without congestive failure.

The blood pressure in hypertensive heart disease generally remains high, but sometimes, either because of spontaneous remission or because of heart failure or general vasomotor collapse, and in some cases evidently aided by treatment, it may fall to average normal or nearly normal levels, leaving obscure the cause of the cardiac enlargement and failure unless knowledge exists of the previous hypertension. The diastolic pressure in such cases may be maintained at a somewhat high level (100 to 110 mm, for example) even though the systolic pressure has fallen to 150 mm or below: this relatively high diastolic pressure and low pulse pressure may in some cases reveal the previous hypertension. In fact, as already noted in the discussion of the clinical classification of hypertension, the systolic level of the blood pressure is far less important than the diastolic so far as strain on heart, arteries, and kidneys is concerned, a rise of a few millimeters of mercury of diastolic pressure is a great deal more serious than several times that rise of systolic pressure. A full pulse pressure with elevated systolic pressure and normal diastolic is common in advanced sclerosis of the larger arteries (with loss of elasticity) and relatively normal arteriolar circulation (that is, without essential hypertension)

It is not known how frequently cardiac enlargement is the result of an old hyperplesia in the absence of hypertension at the time of examination and without evidence of valvular disease, serious coronary disease, pulmonary fibrosis or pericardial disease. Some writers believe that it is always, or almost always, so produced. This is a possibility but by no means a certainty Some causes for enlargement of the heart exist which are not yet clear while others, previously unrecognized, have in recent years been brought to light. More study of this problem is needed.

The systolic pressure in established hypertension varies from 150 to over 300 mm of mercury: it is usually about 200 The diastolic pressure varies from 90 to 180 but is usually 110 to 120 The pressure readings (especially the systolic) vary greatly among different individuals and on different occasions in the same individual. Repeated measurements must often be made before the customary "basal" blood pressure levels for a given patient are dis-

covered, uninfluenced by excitement, exertion, or fatigue. It has been found, as would be expected, that the blood pressure levels recorded by the patient himself or herself at home tend to be distinctly lower than they are in the clinic or doctor's office (Ayman and Goldshine, 1941) It must be remembered, however that neither record is truly representative, and that hyper tension until fixed is likely to go through wide swings from day to day or hour to hour The lability of the pressure is of some importance in prognosis and treatment too, the more favorable cases tending more often to show pressures close to normal. To test the degree of the lability various procedures have been introduced, including especially (1) the *measurement* of the blood pressure *at frequent intervals* day and night, (2) the *cold pressor test* consisting of immersing one hand in ice cold water at 40 F for 30 to 60 seconds, which will cause a mean rise of over 30 mm of mercury in systolic pressure and of over 25 mm in diastolic pressure in hypertensive individuals, or somewhat less in "hyperreactors" (who may some day become hypertensive) and much less in normal nonhypertensive persons (Hines and Brown, 1936) (3) the *sedation test* consisting of the effect of extreme sedation by the ingestion of 3 gr of Sodium Amytal every hour for three doses, the blood pressure dropping to normal in the early or mild and labile cases, and (4) the *postural test* the diastolic pressure rising in hypertensive cases 15 to 30 mm, with less change in the systolic level and hence a drop in pulse pressure readings on assuming the erect position.

A very high diastolic pressure is a bad sign and a constant finding of such a pressure over 130 mm of mercury means that, without special treatment, but a few months or years of life remain. The auscultatory gap found by the auscultatory method of sphygmomanometry (discussed in Chapter 6) and pulsus alternans (to be discussed in Chapter 30) are both common in hyper tension and appear during blood pressure studies. The blood pressure should be measured in spite of the presence of atrial fibrillation an approximate figure so obtained is generally sufficiently accurate. When hypertensive crises occur due to adrenal medullary tumors (pheochromocytomata) or to vasomotor (arteriolar constriction) storms, in the course of chronic hypertension, sometimes with serious effects such as apoplexy the blood pressure may suddenly rise 50 to 100 or more millimeters systolic and half that diastolic.

Special tests for a *pheochromocytoma* have been developed consisting of sharp increase of blood pressure on administration of histamine, Mecholyl, or tetraethylammonium chloride, no reaction to epinephrine, and reduction of blood pressure on intravenous injection of benzodioxane. The more established tests are those with histamine (Roth and Kvale, 1945) and benzodioxane (Goldenberg, Snyder Aranow 1947) The former test consists of determining the basal blood pressure and pulse records after recumbency for ½ to 1 hour then every minute for 15 minutes after the intravenous injection of 0.025 to 0 05 mg of histamine (0.25 to 0.5 cc of 0 01 per cent solution in normal saline) a positive reaction is shown by a sharp rise of blood pressure of 100 mm or more in the presence of a pheochromocytoma in contrast

to a much slighter rise in a case of essential hypertension. The severity of reaction has resulted generally (except when the blood pressure is not n elevated to start with) in replacement by the benzodioxane test, which sists of the intravenous injection in 2 minutes via a normal saline drip operation for 20 to 30 minutes before the test) of 0.25 mg per kilog body weight in 1 per cent solution of piperidymethyl benzodioxane (933 an adrenolytic or epinephrine antagonistic substance a positive reac consists of a considerable fall in both systolic and diastolic pressures in course of a few minutes. Less satisfactory testing for a pheochromocyt includes perirenal air insufflation which can be difficult and dangerous nondiagnostic in some cases when the tumor is situated not at the adr gland but elsewhere along the sympathetic chain, as it sometimes is.

Roentgen ray examination in hypertensive heart disease shows cardiac largement chiefly of left ventricular type (Figure 96 illustration below)



FIG. 96. Roentgenogram showing a moderately enlarged hypertensive heart prominence of the left ventricle. The arc of the descending aorta is well seen abov heart shadow because of its increased density (arteriosclerosis) The pulmonary art is not enlarged, there has been no pulmonary vascular congestion.

general dilatation of the aorta with prominence of both ascending and descending portions in the thorax. Later in the disease, when left ventricular failure begins, greater cardiac enlargement is found, due to dilatation and to involvement of the right side of the heart and of the left atrium then the lung hilus shadows and the pulmonary artery shadow tend also to be prominent, in keeping with the newly developed hypertension in the pulmonary circulation.

Electrocardiography often shows no abnormality in hypertensive heart disease but in the majority of chronic cases there is characteristic hypertensive pattern (Figure 97A) consisting of lowering to inversion of the *T* waves in Lead 1 and in the leads over the left ventricle (V_4, V_5, and V) and of in-

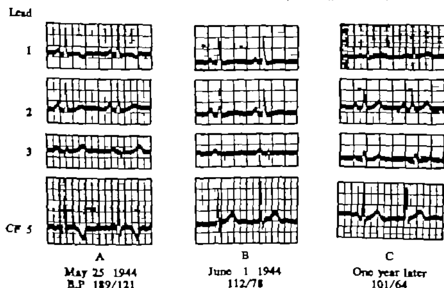


FIG. 97 Reversal of the hypertensive electrocardiographic pattern after lumbodorsal sympathectomy Male, age 39 Lumbodorsal sympathectomy: right side, May 31 1944 left side, June 9 1944

creased amplitude of the *R* waves in these same leads there is frequently also left axis deviation as found in the classical bipolar limb leads, although a horizontal heart position commonly found in hypertensive patients is more responsible for such axis deviation than is left ventricular enlargement. It is likely that dilatation in addition to hypertrophy of the left ventricle is responsible for this abnormality of the electrocardiogram, as borne out by the return to a more normal record in some cases when the hypertension and left ventricular strain therefrom are relieved by splanchnic resection (Figure 98 page 487) Arrhythmias are not the rule but when they appear they are well shown in the electrocardiogram.

Course and prognosis. Hypertensive heart disease tends to be a progressive condition leading sometimes rapidly but usually slowly to congestive heart failure in the course of 10 to 20 years. The condition begins, as a rule, in-

sidiously and very gradually in middle life at about forty to fifty years of age and is often discovered in the course of routine blood pressure or cardiac examination (for life insurance, for example) When it begins in youth it is more serious when it begins in old age it is not so serious unless coronary disease or cerebral arteriosclerosis complicates the condition. Sometimes at first there are merely waves or periods of hypertension with normal pressure be tween. Transient or paroxysmal hypertension may however in the course of time do as much harm to some patients as sustained hypertension in the usual run of cases. Even when the hypertension becomes fixed there tend to be waves or periods of considerable increase above the average level for example, a systolic pressure of 180 mm may rise to 240 for a few hours at a time on excitement, fatigue, or from unknown cause. There may be a mild and temporary increase of blood pressure or an exacerbation of a pre-existing hyper tension at the time of the menopause.

The term *malignant hypertension* has been introduced to designate an ex treme grade of hypertension with a rapidly fatal course (months to a year or two) Actually however it includes a variety of severe cases those that are marked and serious from the very beginning (usually young adults) those approaching the end of a long hypertensive course, and those who after some years of a fairly benign hypertension take a rather abrupt turn for the worse. The chief characteristics of "malignant hypertension are the high diastolic blood pressure (130 to 140 mm or over) the very abnormal eye grounds, and the bad prognosis and rapid course.

Although heart failure is the most common of the end results of hypertension, cerebral hemorrhage is also frequent, angina pectoris and coronary thrombosis are next in order and renal insufficiency is least common. In a series of 410 cases of primary or essential hypertension examined post mortem (Bell and Clawson 1928) congestive heart failure was found in 187 cases (44½ per cent) cerebral hemorrhage or thrombosis in 81 cases (19 per cent) coronary heart disease in 67 (16 per cent) renal insufficiency in 36 (8½ per cent) and miscellaneous conditions in 49 (12 per cent) In a later series (1941) of 2,597 hypertensive patients who succumbed to cardiovascular disease, Clawson found that death was caused by myocardial insufficiency in 43.3 per cent, by coronary heart disease in 36 per cent, by cerebral hemorrhage in 13 9 per cent, and by renal insufficiency in 6.8 per cent. In the series of 375 hypertensive cases studied by Murphy and his associates (1932) heart failure (mostly congestive, but including coronary) caused 50 per cent of the deaths, infections 14.2 per cent, apoplexy 13 4 per cent, and renal failure 10 4 per cent. Fahr (1935) put the percentage of deaths in hypertensive cases due to congestive heart failure at 55

Serious prognostic signs are very high diastolic blood pressure (over 130 mm) marked changes in the eye grounds, pulsus alternans, gallop rhythm, and paroxysmal dyspnea or cardiac asthma A serious prognosis should not be given on the finding of slight or moderate hypertension or slight cardiac

enlargement alone. Much cardiac enlargement or sustained hypertension of very high degree warrants a grave prognosis.

On the other hand, within the last decade a change has taken place in the course and probable prognosis of some of the cases of hypertension, even of high grade with hypertensive heart disease, as the result of the more complete splanchnic sympathectomy carried out by Smithwick (1940 and observations made by myself on his cases, 1942–1951) Occasionally striking results have occurred with relief not only of the hypertension, eye ground changes, and symptoms but also of the physical and electrocardiographic evidences of the heart strain, such as gallop rhythm, pulsus alternans and *T* wave abnormalities. In at least a few of these cases the hypertensive heart disease should be regarded, like the thyrotoxic hearts and some instances of acute rheumatism, as a reversible process in its acute or subacute stage. The strict application of low sodium and of Kempner's rice diets has also reversed or retarded the hypertensive process in some, though relatively fewer cases.

Complications. The most important complications of hypertensive heart disease, and their relative frequency have been noted above congestive heart failure, apoplexy angina pectoris, coronary thrombosis, and nephritis with uremia. Acute infections are common and may end the story as may also pulmonary embolism from phlebothrombosis in the leg, especially after congestive heart failure has set in. Arteriosclerosis is almost universally found in older patients with hypertension, but, although undoubtedly favored by the strain of the high blood pressure, it is not by any means a constant finding. Types of heart disease other than that due to coronary sclerosis may complicate the enlargement and weakness from hypertension. Syphilitic aortitis, thyrotoxicosis, and rheumatic heart disease are not infrequent complications. Hypertension is often found with aortic regurgitation and with mitral disease, with or without much stenosis, and it is not rare even with aortic stenosis. Finally nervousness and neurocirculatory asthenia are common complications of hypertensive heart disease and frequently exaggerate the seriousness of the symptoms and of the condition itself.

Treatment. The treatment of hypertensive heart disease resolves itself into three parts, consisting of (1) the therapy of cardiac complications, (2) the therapy of the underlying hypertension, and (3) preventive measures to protect the damaged heart.

(1) The treatment of the cardiac complications, such as congestive failure, cardiac asthma, angina pectoris, coronary thrombosis, and atrial fibrillation will be discussed in later chapters of this book, mainly in Part IV The presence of hypertension does not in any way contraindicate the usual measures, as, for example, the use of digitalis for failure or for atrial fibrillation, of nitrites for angina pectoris, of morphine for coronary thrombosis and cardiac asthma, and of quinidine for atrial fibrillation. It need hardly be added that the most important measure of all, not in the emergency but when the emergency is over is an attempt if it seems feasible by medical or surgical measures

(outlined below) even in the absence of specific therapy to reduce the main factor of strain, namely the hypertension.

(2) The treatment of the hypertension itself continues to be a difficult task in the present state of our knowledge, but important studies in progress offer much hope for the future.

Drugs. Many measures, especially medicinal, to reduce high blood pressure, have been suggested and tried, sometimes with slight temporary success, sometimes with toxic effects, sometimes though rarely with prolonged benefit; these include such drugs as the nitrites, bismuth subnitrate, benzyl benzoate, atropine, calcium chloride, potassium iodide, bromides, parathyroid preparations, theobromine, theophylline ethylene diamine (called also aminophylline, and formerly Euphyllin or Metaphyllin) theobromine sodiosalicylate (Diuretin) theobromine sodium acetate (Thesodate) and other diuretics, cucurbocitrin (from watermelon seeds) papaverine mistletoe (intrait de gui) sunflower seeds, garlic, yohimbine, liver extract, ovarian extract, testosterone, chloral hydrate and other sedatives or hypnotics like phenobarbital (Sodium Luminal) cathartics, sulphur and the sulphocyanates (thiocyanates) of sodium or potassium. In one series of 70 patients with established essential hypertension (Evans and Loughnan, 1939) the effects of 33 different preparations and of a placebo on the blood pressure and on the symptoms were observed. None produced a satisfactory hypotensive effect. Symptomatic improvement greater than that resulting from the placebo followed the use of only six of the drugs, namely bismuth subnitrate, iodine and iodide bromide, Sodium Luminal (phenobarbital) Theominal (theobromine and phenobarbital) and potassium thiocyanate. The sedative drugs seemed to have value in temporarily relieving nervous symptoms when these were prominent, and since it is now well established that heavy sedation (e.g., Sodium Amytal 0.2 gm, 3 gr every hour for three doses) frequently reduces hypertensive blood pressure readings markedly even to normal, there is an additional good reason therein for the therapeutic use of sedative drugs.

There has been in recent years a revival of the use of the thiocyanates (sulphocyanates) and of veratrum viride and various of its derivatives which appear to be more effective in reducing the blood pressure and in relieving symptoms in hypertensive patients than do other drugs. However their effect has been often disappointing and sometimes seriously toxic. They should be used under close observation, best controlled in the case of the thiocyanates by frequent measurements of the concentration of the drug in the blood itself (preferably kept at 6 to 12 mg per 100 cc blood)

Veratrum viride has been in use for many years in the treatment of eclampsia, frequently with considerable reduction of blood pressure but complicated by toxic symptoms. The drug under various trade names has been in use also for some time in the treatment of essential hypertension with similar results. An analysis of its effects has been published by Freis and Stanton (1948) Only recently have satisfactory extracts been made from veratrum in the form of purified alkaloids. One of these, called protoveratrine from Vera-

trum album has given much promise as indicated by its uniform reduction of both systolic and diastolic pressures for several hours at a time without serious toxic symptoms in hypertensive animals and man when given parenterally (Meilman and Krayer 1949) More recently still protoveratrine has been given orally to ambulatory patients with beneficial effects over periods of weeks and months, but the dosage has to be very carefully regulated for each individual to obtain the best hypotensive effect with the least toxic result. The dosage parenterally varies from 0.25 to 1 0 mg every 6 hours and orally from 0.5 to 2.0 mg every 8 hours. This drug has proved to be especially useful in patients who are too old or otherwise unsuitable for lumbodorsal sympathectomy Whether or not protoveratrine or some other even more effective medicament can actually replace operative treatment it is too early to say It should be added that the heart rate as well as the blood pressure is considerably reduced by veratrum derivatives, even down to 40 per minute

Other derivatives from veratrum viride that have been used somewhat helpfully in cases of hypertension are Vertavis (15 to 30 Craw units daily) and especially Veriloid which can be given in the dosage of 2 to 3 mg orally every 6 hours (Wilkins, Stanton, and Freis, 1949 Connar Emlet, and Grimson, 1950) It may be added that atropine should be available to counteract toxic effects from any veratrum preparation.

Potassium thiocyanate is conveniently given in the form of a 4 to 8 per cent solution in peppermint water or in a simple syrup such as that of sarsaparilla, and in the dosage of one teaspoonful (4 cc) containing 0 16 to 0 32 gm (2 to 5 gr) three times a day (total of 0.5 to 1 0 gm or 7½ to 15 gr) the dosage varies as circumstances warrant. In one of the largest group of cases reported, that of 246 by Barker and his associates (1941) symptoms were relieved and blood pressure was reduced in 47.5 per cent in the course of two to four weeks. In another series of 50 patients subjective improvement was definite in 63 per cent, fair in 20 per cent, and disappointing in 17 per cent, six showed toxic effects the blood pressure of every patient was somewhat reduced, and objective results were considered satisfactory in 78 per cent, fair in 16 per cent, and poor in 6 per cent, the average systolic pressure dropped from 197 mm before treatment to 156 mm with treatment, and the average diastolic pressure dropped from 115 to 94 the average maintenance dosage of 5 gr varied from three to twenty-one (average nine) times per week. In another group of 20 patients with pronounced arterial hypertension (Blaney Geiger and Ernst, 1941) to whom potassium thiocyanate was given after a control period on placebos, one half of the total number apparently responded with a complete or partial remission of their hypertension eight of the 16 patients with symptoms felt better during the therapy a few felt worse. In still another group 120 hypertensive patients were treated (Caviness and associates, 1941) with results recorded as good in 68 9 per cent (reduction of more than 15 per cent in both systolic and diastolic pressures) fair in 11 5 per cent, and poor in 19 6 per cent. Other authors, however have emphasized the toxic effect of the drug (Wald, Lindberg, and

Barker 1939 Robinson and O'Hare, 1939) the last-named authors reported toxic symptoms in 29 (38 per cent) of their 75 patients, less serious in 23 of them (nausea, weakness, dermatitis, purpura and a decrease in libido) and more serious in the other 6 (dermatitis exfoliativa, congestive heart failure, cerebral thrombosis, angina pectoris, and psychoses) but at the same time they believed that there was decided value in the therapy when carefully controlled (maximum drops in blood pressure of over 100 mm systolic and 35 mm diastolic were observed in 3 cases, average drops of 40 mm systolic and 20 mm diastolic in 63 per cent of the patients, and relief of hypertensive headaches in 18 out of ₄0 cases)

Rogers and Palmer (1947) compared the use of thiocyanate therapy in hypertension to sympathectomy by Smithwick s operation, they found that only about one fifth of 100 patients showed any considerable fall in blood pressure from the effect of the drug and that such falls required continuous therapy for their maintenance and were not at all comparable to the drop in pressure obtained in favorable cases by splanchnic resection once in a while, however the drug produced brilliant results in the relief of headache.

Recent papers on the administration of the thiocyanates emphasize a general dissatisfaction with their use (Ruskin and McKinley 1947) and their greater value in the absence of organic changes (Alstad, 1949)

Other drugs more recently introduced with definite hypotensive but generally disappointing effects include tetraethylammonium chloride, dihydroergocornine derived from ergot, Dibenamine, and Driscol. Still other medicaments recently recommended but unconfirmed include procaine HCl in honey thyroid extract, and Rauwolfia serpentina. Rutin, a flavone rhamnoglucoside extracted from wheat germ has been used to reduce the hazard of hemorrhage from capillary fragility in essential hypertension but there has been considerable doubt as to its clinical value.

Most recently hexamethonium salts have been tried for hypertension (Smirk, 1951 Locket, et al. 1951 George W Pickering, personal communication, 1951) it appears to be effective if given intramuscularly 3 or 4 times a day at increasing dosage beginning with 15 mg.

Diet. Dietary restrictions have been tried, particularly the limitation of the total caloric value of the diet, of protein food, and of common salt. Reduction of weight has been carried out with some benefit in a good many obese patients reference has already been made earlier in this chapter (page 468) to the hypotensive effect of starvation with resulting loss of weight.

Two special diets are in common use today in the treatment of hypertension because of their success in some, though in the minority of cases. One of them introduced years ago emphasized the need of restriction of sodium chloride (Allen, 1920) and has been resumed and studied in recent years with variable success. It has been shown that it is the sodium content of the diet that is important, as it is in the case of the dietary treatment of congestive heart failure· in fact, it is the hypertensive patient with congestion threatened or present who receives the most benefit. Just how on occasion the sodium re-

strictron acts on hypertension has not yet been elucidated its relationship to adrenal function among other mechanisms has been indicated.

The other diet which in recent years has been much utilized in the treatment of hypertension is the rice diet introduced by Kempner (1944) In the first place, this diet has about as low a sodium content as it is possible to give (less than 0.5 gm) secondly it is very low also in protein (about 20 gm daily) and, thirdly it contains very little fat (about 5 gm daily) It consists of rice, fruit, and sugar with no other food during the first six weeks or more of treatment but later is liberalized according to circumstances. The explanation of its success is still unclear but in those persons who are faithful to it (a minority of cases) there is an improvement of abnormal eye grounds, electrocardiogram, and heart size, and a definite reduction in blood pressure, both systolic and diastolic, in more than half (the exact percentage has not yet been determined) whether or not there has been a loss of weight. There need be no weight loss since the diet contains at least 2,000 calories. As in the case of the low sodium diet, so here too it is the somewhat congested hypertensive patient who seems to receive the most benefit, and also some cases of renal involvement, for whom as a matter of fact the diet was first introduced.

It should be emphasized that the conscientious following of this rice diet" has been helpful in the case of many hypertensive patients, including some not improved by other therapeutic measures, medical or surgical, including sympathectomy also that it can be added helpfully to other treatment not sufficiently effective per se.

Much study remains to be done on the effect of diets on hypertension, and it is to be observed also that on occasion there may develop, from either of the diets noted above, a serious sodium lack requiring emergency treatment.

Other medical measures. Measures of physical therapy have been advocated rest, physical and mental baths of all kinds venesection electrotherapy (high frequency diathermy) and roentgen ray irradiation of the pituitary and adrenal glands. Psychotherapy has been used both consciously and unconsciously along with attempt to adjust or to remove strain of professional or business life, of family affairs, and of social activities. Often these measures have been combined in various ways and degrees, particularly at special health resorts or spas, and often by the family doctor or specialist at home.

The imposing list of remedies and their advocacy by so many different persons reveal their very weakness we have not yet a real cure or a specific treatment for hypertension except, on the one hand, surgical removal of certain unilaterally diseased or deformed kidneys and pheochromocytomata in rare cases and, on the other hand, thoracolumbar (lumbodorsal) sympathectomy in suitable cases. Whether to match the numerous causes of hypertension, we may have to develop a variety of cures, or whether a single drug or chemical or other measure will neutralize hypertension in the majority of cases no matter what the original cause, we do not yet know

Rest either per se or enforced by a stay in a hospital or in bed at home, as the result of some illness or surgical operation, sometimes materially lowers

a high blood pressure, even temporarily to normal if it is not too high to start with, but rarely is this effect maintained after the patient has become active again, in contrast to the more lasting effect of lumbodorsal splanchnic resection when it is successful, as will be recounted below (Rojas, et al., 1944)

Summarizing the value of the various methods of medical treatment it may be said that a few have been shown to be more useful than others, not as cures, but in a palliative way These are (1) a relief from all avoidable nervous and physical strain, sometimes in the form of "rest cures, but not an interdiction of moderate healthy outdoor exercise, (2) a general reduction of diet, not to a weakening starvation level but to one that prevents gain of weight or causes a moderate, gradual loss of weight if there is obesity as there so often is in hypertensive cases and especially a reduction of sodium intake as in the rice diet (see above) (3) symptomatic or specific treatment of any particular complicating diseases or disorders, including the eradication of such foci of infection as apical tooth abscesses, (4) the trial of nerve sedatives, and (5) the use of the more successful drugs, namely potassium thiocyanate and especially the Veratrum derivatives under careful control, as already described. Sometimes none of these measures has any effect whatsoever Slight oscillations of blood pressure must not be regarded as important indications of the effect of treatment. Relief from all avoidable nervous and physical strain, with a healthy regulation of rest, exercise, diet, and bowel action, is of prime importance and sometimes not possible at home where business, social, and family cares are hard to escape. A holiday in some pleasant place or a visit to a good health resort at home or abroad may do much good under such circumstances. But whether carried out at home or at a health resort a fall in blood pressure, though rarely to normal levels not infrequently follows such therapy

Surgery In late years there have been introduced for the treatment of hyperpiesia certain surgical procedures Decortication of the kidneys has proved ineffective. Excision of a deformed or diseased kidney (especially the site of cystic or pyelonephritic degeneration) with the other kidney fairly normal has cured the hypertension in a few cases, justifying, though to a small degree only the hopes from such a procedure based on the effect of the vascular clamp in experimental animals pleas have been made for conservatism in such surgery so that useful renal tissue may not be sacrificed in vain. Extensive bilateral thoracic and lumbar rhizotomy though reported to be effective, is too serious and dangerous an operation. The value of adrenal denervation and of subtotal adrenalectomy is now being investigated. A few spectacular cures have resulted from the exploratory discovery and removal of adrenal tumors (especially the pheochromocytoma responsible for severe paroxysmal hypertension)

Sympathectomy including splanchnic nerve resection (bilateral) introduced with the idea of causing a drop in blood pressure as the result of splanchnic and lower limb arteriolar dilatation, has been developed to a high degree by a number of surgeons (Peet and associates, 1935 1940, 1948 Adson and Allen, 1940 Smithwick, 1940 1948 de Takats and associates, 1942,

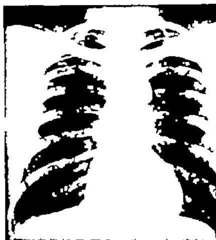
1948 Crutchfield, 1947 Poppen, 1947 Grimson and Orgain, 1948) some of whom, most notably Smithwick, now denervate both above and below the diaphragm with the result that more and more patients have secured and maintained a distinct hypotensive effect (so great in some cases that at first syncope or near-syncope may occur in the erect posture) Smithwick (1940 1942) stated that removal of virtually the entire great splanchnic nerve with division of all of its aortic branches coupled with interruption of the communicating rami of D9 D10 D11 D12, and L1 together with excision of the sympathetic trunk over this area, is the minimal procedure found consistently to produce a blood pressure change which is characteristic of a thorough interruption of the nerve supply to the splanchnic bed. The younger patients with more labile vasopressor reactions, smaller pulse pressures with relatively higher diastolic than systolic levels, and less permanent cardiovascular damage have been found most amenable to improvement even though their pressures may be elevated and their fundi seriously affected (and as such belonging to the "malignant hypertensive" category) Spectacular improvement (perhaps cure) has been noted now in a good many cases but the procedure is still relatively new and has but recently emerged from the experimental stage.

Among 224 cases sympathectomized at the Mayo Clinic (Allen and Adson, 1940) good results were reported in 13 per cent, fair in 18 per cent, temporary in 39 per cent, and poor in 30 per cent. With improved technic, consisting for the most part of more extensive sympathectomy better results have been obtained since 1940 Among the larger series of cases treated by experienced surgeons and with better selection than originally the results have been well worthwhile in slightly over half the patients operated upon and followed for several years. For example, in Smithwick's series of 256 patients with essential, including malignant, hypertension operated upon by his newer technic between 1938 and 1943 and followed for five to nine years, the total mortality was 31 2 per cent, distinctly less than the expected rate for similar hypertensive cases not so treated, 90 per cent of the survivors were improved symptomatically the eye grounds were improved in 41 per cent, the electrocardiograms were better in 42 per cent, and the blood pressures were lower in 47 per cent (Smithwick, 1948) During the first five year follow-up study 84 per cent of the cases had shown a distinct lowering of pressure, but a considerable number of these showed a gradual return of blood pressure toward or to the preoperative levels during the later (5 to 9 years) follow-up period. Palmer (1947) reported a diminishing return of favorable results the longer the patients are followed, nearly 70 per cent early in his experience, declining to 25 per cent when patients are followed three to five years or more. "But," he writes, "this effect has been obtained twice as frequently in this series by surgical means as by a careful medical regimen and was obtained in patients with malignant hypertension whose blood pressures were unaffected by medical management." Isberg and Peet (1948) have reported that 60 per cent of 384 cases of arterial hypertension were alive 5 to 12 years after splanchnicectomy of the survivors, 41 per cent of those with abnormal electrocardiograms showed improvement, and 44 per cent of those with preoperative

cardiac enlargement showed significant decrease in heart size. Another series of 100 consecutive patients were treated by extensive thoracolumbar sympathectomy by the same surgeon and carefully followed for 1½ to 4 years after operation the results were good in 47 per cent, fair in 24 per cent, and unsatisfactory in 28 per cent, including one operative death and six others who died after discharge from the hospital (Poppen and Lemmon, 1947) Grimson and his associates (1949) have reported the results of subtotal to total sympathectomy in 113 patients with severe or moderately severe hypertension followed for one to nine years 97 of the cases were still living with normal or near normal blood pressure in 31 reduced pressure in 43 more, and postural lowering of pressure in all, together with improvement in eye grounds in many cases and in electrocardiograms and heart size in a few

I myself have seen many excellent results among the cases sympathectomized by Smithwick not only have the eye grounds cleared and the pressure fallen to normal or near normal but evidences of heavy strain on the heart have also abated, including electrocardiographic abnormalities (Figure 97 page 477) (Canabal, Thomson, and White, 1944 White, et al. 1945) and even on occasion x-ray evidence of cardiac enlargement (White, 1946, and Figure 98) My own most interesting experience in the treatment of serious hypertensive cardiovascular disease has been summarized in a personal study of 100 cases with important complications, including for the most part left ventricular weakness or frank failure, but also cerebral vascular lesions, angina pectoris, and past myocardial infarction. Fifty of these cases had thoracolumbar sympathectomy by Smithwick; the other cases (controls) of similar sex and age distribution (ratio of 3 men to 1 woman and large majority of cases under the age of 50 in each group) and with similar defects had medical but not specific dietary treatment. Each group was followed for a minimum of three years. The mortality in a given period of time of the surgical group was less than half that of the medical group and the blood pressures, eye grounds, electrocardiograms, and symptoms were normal or much nearer normal in the majority of the survivors of the surgical group than in the controls. The surgical cases who were not helped at all or who were worse or died were further analyzed, one patient who had been improved died later of leukemia while 12 of the other 29 cases who died or were not improved could in retrospect have been quickly rejected for sympathectomy by the application of new criteria recently introduced by Smithwick (1950) in which a scoring of adverse points for various abnormalities is made and then the points added up (scores under 4 more suitable for operation than those above) For example, an abnormal electrocardiogram is one adverse point, x-ray evidence of cardiac enlargement another age of 50 years a third, and so on. Abnormality of renal function is especially serious and in general a contraindication to surgery· moderate involvement of the heart, however or a cerebral vascular lesion is not a bar per se. The borderline group (Smithwick's Group 3) contained 19 of my 50 sympathectomized cases, 10 of which turned out well and 9 poorly it is now this group that especially needs further evaluation.





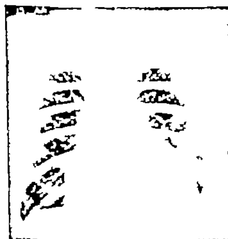


FIG. 98. Roentgenograms of thorax of patient with hypertensive heart disease. (*A*) Film showing marked cardiac enlargement of hypertensive heart in severe congestive failure. (*B*) Film of same individual after clearing of congestive failure. (*C*) Film of same individual sixteen months after lumbodorsal sympathectomy which had reduced the blood pressure from an average preoperative level of 227 mm systolic and 120 mm diastolic to 155 mm systolic and 97 mm diastolic.

The fact that 5 of my 50 hypertensive cases with grave cardiovascular lesions were perfectly well with normal blood pressure three years or more after operation and that 15 more were distinctly improved is quite clear proof, in my experience, that hypertensive cardiovascular disease is reversible and that up to the present time sympathectomy has achieved the greatest therapeutic success in this respect.

It must be clearly recognized, however that this surgical treatment is largely empirical and may be replaced or reinforced later by something better that it is a serious major operative procedure in itself (in fact, two operations, first on one side and then on the other ten days to two weeks apart) that it is followed by a tedious, often uncomfortable, convalescence lasting two or three months, and that it is not suitable for the majority of patients with hyperten-

sion. Many cases are too old (an age under 50 years is desirable) some patients are too sick (especially if they have important kidney disease or renal insufficiency) some cases are too mild (with mostly a nervous or transient hypertension which should be watched) and many cases have mostly an arteriosclerotic hypertension with high systolic pressure (over 200 mm) and relatively low diastolic pressure (about 100 mm) allowing long survival and *not requiring or appreciably helped by sympathectomy* But for particular cases, especially young and middle-aged men with malignant hypertension and good renal function sympathectomy can be lifesaving. Such indication applies of course to well under 10 per cent of all hypertensive patients.

Thus, as I stated seven years ago in the third edition of this book, Smithwick's work represents a notable advance in the control of hypertension though we may hope that some simpler therapy or preventive measure will eventually replace operative treatment.

Finally it must be said that a survey of many cases showing the serious late effects of chronic hypertension makes it evident that early discovery of hypertension at its origin by annual examinations affords the only promise for control of the disease by the earliest application of the measures outlined above, until someone discovers a specific, perhaps antitoxic, cure. Such a cure is being sought in the work of Page and his colleagues (1940, 1949) Ferris, et al. (1948) Goldblatt (1948) Schroeder (1948) Krayer and Mellman (1949) Wilkins (1949) Smithwick (1949) Chasis, Goldring, and Smith (1949) and many others. The work is, however very arduous and difficult and much patience must be exercised in awaiting the final results.

(3) The care of a patient with hypertensive heart disease, aside from the treatment of cardiac complications and hypertension already mentioned, is like that of any chronic cardiac patient a reasonable restriction of activity and nervous strain, common sense as to diet, exercise, and rest, occasional or frequent leisurely holidays, regulation of bowels, avoidance of excessive use of alcohol, tobacco, coffee and tea, and the eradication of focal infection. It is, however of the greatest importance to recognize the possibility of the reversibility of even serious hypertensive heart disease by therapy at present best exemplified in the surgical procedure of sympathectomy

Finally it is of prime importance to practice preventive medicine in hypertensive families by instructing both young and old concerning the establishment of sensible health habits.

Differential diagnosis. Hypertensive heart disease is generally easy to recognize because of the presence of hypertension and of cardiac enlargement without valvular disease. The onset of dilatation of heart and aorta sufficient to cause mitral and aortic systolic murmurs, the occurrence of atrial fibrillation, the masking of the original condition by the presence of marked congestive heart failure, and especially the fall of blood pressure to normal levels may make it very difficult or even impossible to distinguish some cases of hypertensive heart disease from chronic coronary heart disease in which the history is atypical or obscure, and from cardiac enlargement and failure due to

thyrotoxicosis or even to chronic rheumatic or syphilitic valvular disease. A careful history to rule out rheumatic and syphilitic infections, knowledge of physical examinations in the past which have not shown evidence of valvular disease or thyrotoxicosis, and especially careful inquiry as to a previous discovery of hypertension are often more essential in this differential diagnosis than are physical examination and laboratory tests carried out at the moment when the decision must be made.

HYPOTENSION

Hypotension, that is, a systolic blood pressure below 100 mm of mercury does not cause heart disease although it sometimes accompanies it, as in the case of aortic stenosis or acute heart failure from cardiac infarction (due to coronary thrombosis) Low blood pressure is more commonly found in the absence of heart disease than in its presence especially in certain weak and frail individuals, in chronic wasting disease, temporarily in peripheral vascular failure or shock (see Chapter 31) or in attacks of neurocirculatory asthenia or of paroxysmal tachycardia with excessively rapid heart rates, in a few cases of marked carotid sinus reflex in the rare cases of adrenal (Addison's) disease, and in a few individuals as a postural phenomenon where it has been called orthostatic or essential hypotension.

Postural hypotension has been called a disease of the sympathetic nervous system by Stead and Ebert (1941) whether peripheral or central is not clear though the latter is favored (Hermann, 1947) Patients with this condition do not apparently pool more blood in the lower part of the body on standing than do normal subjects, but they lack the reflex vasoconstriction which maintains the arterial pressure in normal subjects when erect this phenomenon may appear acutely and temporarily in healthy persons after very strenuous exercise (Eichna, et al., 1947) and it is, of course, quite common for a few weeks after thoracolumbar sympathectomy for hypertension.

An abdominal support, elastic stockings, paredrine (Yukis and Griffith, 1948) and angiotonin, and the head-up bed (Corcoran, et al. 1942) have given relief.

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CHAPTER 20

PULMONARY HEART DISEASE
ACUTE AND CHRONIC COR PULMONALE
PULMONARY HYPERTENSION

Introduction. During the past seven years since the publication of the third edition of this book there have been distinct advances both in the clinical recognition of the frequency of pulmonary embolism in medical, especially cardiac, cases, along with better diagnostic criteria, and also in the introduction of preventive measures, thus reducing the incidence of the complication of the acute cor pulmonale. Also, the application of improved industrial hygiene and of more specific measures to reduce pulmonary infections will doubtless result in time in a decreased incidence of the chronic cor pulmonale.

The effect of pulmonary hypertension on the right ventricle is comparable to that of systemic hypertension on the left ventricle, except that in the case of the pulmonary circulation there are more instances of *sudden unexpected* great increase in blood pressure to cause acute right ventricular strain. Pulmonary hypertension originates in the great majority of cases in seven different ways. In the first place and most commonly from dilatation and failure of the left ventricle, abrupt or gradual, secondly and fairly often, from mitral valve deformity with or without stenosis, thirdly and also frequently and always abruptly from massive pulmonary embolism, fourthly and usually to but a slight extent, from chronic pulmonary disease, including fibrosis and emphysema, fifthly importantly but not often, from the pressure of inhaled dust, in particular silica, sixthly from the more marked grades of chest deformity due to high degrees of kyphoscoliosis or compression (not displacement) of the heart by the "funnel chest" and, finally and rarely from primary disease of the pulmonary arteries and arterioles. There are also excessively rare instances of acute, subacute or chronic cor pulmonale secondary to obstruction of the pulmonary circulation by metastatic malignancy or by high degrees of diaphragmatic herniation with compression of the thoracic contents by stomach and intestines.

The first factor, left ventricular dilatation and failure, will be discussed in

Chapter 30 on Congestive Heart Failure the second factor mitral valve deformity will be discussed in Chapter 26 on Valvular Disease. The third factor pulmonary embolism, in its relationship to the heart will be discussed in the present chapter under the heading *the acute cor pulmonale* The fourth factor chronic pulmonary disease, if extensive and prolonged enough, gives rise to a cardiac condition which used to be called "the emphysema heart," but which along with the cardiac effect from the fifth, sixth and seventh factors, namely pneumoconiosis, marked thoracic deformity and pulmonary endarteritis obliterans, will be discussed below under the far superior designation, *chronic pulmonary heart disease* or *the chronic cor pulmonale*

Incidence. This condition—cor pulmonale or pulmonary heart disease—is an important one, though variable in incidence in different parts of the world. It has been considerably neglected and is probably more common than most statistical studies at present indicate, especially since it occurs so often in older people who are not frequently seen in general hospitals which treat acute conditions. In New England its chronic form was noted 21 times (0.9 per cent) in 2,314 cases of organic heart disease (White and Jones, 1928) but in certain places like Vienna (Erdheim, personal communication, 1929) and Cleveland (Scott, 1941) it is either more common or better recognized, Scott noted it in 6 8 per cent of 790 cases who died of heart disease in Cleveland. Two groups of cases of chronic cor pulmonale studied at autopsy have been recently reported, 60 by Spain and Handler in 1946 and 42 by Spatt and Grayzel in 1948 Of 123 collected cases analyzed by Sodeman (1948) 75 were associated with emphysema, 14 with bronchial asthma, 13 with silicosis, 5 of which had also tuberculosis, 9 others with tuberculosis, 7 with bronchiectasis, and 1 each with kyphoscoliosis, pulmonary arteriosclerosis, pulmonary fibrosis, and schistosomiasis. The incidence of the acute form is more common than was previously recognized, being found in about 10 per cent of cases of acute pulmonary embolism but is probably present in additional cases though masked by other signs, e g., coronary insufficiency In slight degree it is not uncommon in high degree it appears to be rather rare.

ACUTE AND SUBACUTE COR PULMONALE

Etiology *Cause* Sudden massive obstruction of the pulmonary circulation sufficient to cause dilatation of the right ventricle gives rise to the condition which we have called *acute cor pulmonale* (McGinn and White 1935) The cause of such sudden massive obstruction of the pulmonary circulation is in the great majority of cases extensive pulmonary embolism originating from systemic venous thrombosis usually in the leg veins. Conceivably a large embolus may also come from the right atrium, but this is much less common, as is likewise embolism from pelvic and abdominal veins. Sudden perforation of an aortic aneurysm into the pulmonary artery can raise the pulmonary arterial pressure so abruptly that doubtless acute dilatation of the right ventricle antedates the inevitable death that ensues. Also an acute compression of

the lungs by a sudden increase of a herniation of the abdominal contents through the diaphragm has been reported as a cause of the acute cor pulmonale (McGinn and Spear 1941) as has likewise acute spontaneous mediastinal emphysema (Klein, 1947) Pneumonia and other pulmonary infections do not give rise to the acute cor pulmonale.

Age The acute cor pulmonale is found in the great majority of cases in older persons, that is, in just those most subject to pulmonary embolism It is rare under 35 years of age

Sex Both sexes are about equally affected.

Predisposing factors By far the most important predisposing factor is systemic venous thrombosis in the deep veins of the calf, leading to involvement of the femoral veins, or in the long saphenous veins, whence multiple and often lengthy emboli are carried to the lungs favoring such thrombosis are stasis and phlebitis in individuals who have had a surgical operation (especially an abdominal or pelvic operation) or an accident or leg injury or any prolonged illness within a few weeks of the time of the occurrence of the pulmonary embolism. Flabby musculature a prolonged cramped position, especially seated with pressure under the knees, and poor local circulation in the legs increase the likelihood of a venous thrombosis and pulmonary embolism under the conditions just mentioned.

Pathology The only characteristic pathologic findings in the case of the acute cor pulmonale are dilatation of the pulmonary artery dilatation of the right ventricle and obstruction of the pulmonary artery or arteries usually by a single coiled massive embolic thrombus but sometimes by multiple emboli. There must be a sudden blocking of at least 60 per cent of the pulmonary arterial circulation before the normal right ventricle dilates appreciably to effect this there must be either a large rider embolus at the bifurcation of the pulmonary artery or at least two large emboli, one in each lung.

There may or may not be congestive heart failure complicating the right ventricular dilatation. At autopsy there may be little or nothing found wrong with the right heart because of the possibility of rapid subsidence of the functional cardiac dilatation, especially if death has resulted finally from a state of vascular shock.

Careful search at postmortem examination will almost always reveal extensive thrombosis in a long leg vein most often the superficial femoral or the saphenous, which is frequently not evident during life.

Symptoms. There are no particular symptoms of the acute cor pulmonale per se except that some of the substernal oppression that attends the acute pulmonary embolism or resulting coronary insufficiency in an older person may possibly be attributed to the acute cardiac dilatation. Any other symptoms are likely to be masked by the severe symptoms from the pulmonary embolism itself the state of shock, sudden air hunger oppression in the chest, cough, weakness and sometimes syncope Substernal oppression due to a complicating angina pectoris or even to a secondary acute myocardial infarction occasionally appears. Later symptoms, if there is survival for twelve hours or more,

may include epigastric discomfort from liver engorgement secondary to heart failure and fever and pleuritic pain due to the pulmonary infarction which is not at first evident.

Signs. Signs of the acute cor pulmonale include evidence of increase in size of the right ventricle, of dilatation of the pulmonary artery and sometimes of failure of the right heart. Such signs may be transient or modified because of the coincident occurrence of coronary insufficiency or of vasomotor shock which reduces markedly the return of blood to the right heart and so prevents much dilatation thereof.

Characteristic signs related to the pulmonary artery dilatation that have been reported are forceful pulsation of the pulmonary artery evident both by inspection and by palpation, along with increased percussion dullness at the left upper border of the heart, marked accentuation of the pulmonary second sound, a loud blowing pulmonary systolic murmur and a to-and-fro friction rub over the pulmonary artery very superficial and probably due to the pressure of the bulging artery and infundibulum against the pericardium underlying the sternum.

Signs indicative of right ventricular dilatation and failure include increased percussion dullness, diastolic gallop rhythm at the lower end of the sternum, and engorgement of the neck veins with or without pulsation. There may even be some engorgement of the liver

An interesting and important finding is that of an abnormal electrocardiogram which is characteristic and apparently pathognomonic an *S* wave develops in Lead 1 the *T* wave in Lead 2 tends to be low or inverted, a *Q* wave develops in Lead 3 or is increased in amplitude, the *T* wave in Lead 3 is quite deeply inverted and in the precordial leads over the right ventricle, in particular V_2 and V but also at times V_4 the *T* waves are flattened or more often inverted (Figure 99) These electrocardiographic changes come and go rather quickly along with changes in the condition of the patient· they are for the most part attributable to the acute dilatation of the right ventricle and not so much to anoxemia secondary to the pulmonary embolism itself However they are often masked or replaced in older patients with important degrees of coronary heart disease by patterns of coronary insufficiency or of myocardial infarction.

It is important to note that most instances of pulmonary embolism are not attended by the acute cor pulmonale, chiefly because the obstruction of the pulmonary circulation is not of high enough degree hence in only a minority of cases of pulmonary embolism should one expect to find the characteristic electrocardiogram It was present in variable degree in 33 out of a series of 92 patients recently studied by the author but well marked in less than half of these, making a total of about 10 per cent of the entire series (Murnaghan, McGinn, and White, 1943) There are therefore normal electrocardiograms in a large percentage of cases of pulmonary embolism, although some have abnormal records due to pre-existing heart disease (especially coronary) further affected by the strain of the new vascular accident, and in still others there are

suggestions of a slight degree of the acute cor pulmonale with or without underlying heart disease. It is of further interest to note as we have found, and as has been pointed out by Currens (1942) that myocardial infarction may be precipitated by the strain and anoxemia secondary to pulmonary embolism,

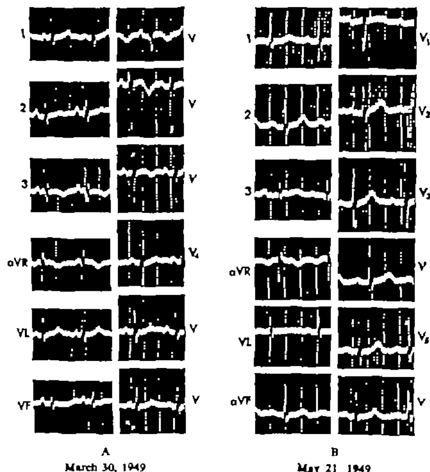


FIG 99 Electrocardiograms in case of acute cor pulmonale, female, age 65 (*A*) Bipolar limb leads 1, 2, and 3 unipolar limb leads, VR, VL, and VF and six precordial leads, V to V inclusive. (*B*) Same, several week after operation with removal of clot from leg vein. Time = 0.04 and 0.20 second amplitude 1 mm = 0.10 mv

especially in older persons with less adequate coronary circulations. If such an infarct is in the posterior wall the electrocardiographic pattern may be at first confused with that of the acute cor pulmonale, or the two may be superimposed, as may also be the patterns of anterior myocardial infarction and the acute cor pulmonale. Even without actual infarction a temporary state of myocardial anoxia may alter the electrocardiogram but it will not produce

the pattern of the acute cor pulmonale It is always important to explore the precordium electrocardiographically in the second and third positions over lying the right ventricle in the search for abnormality that is, flattening or inversion of the *T* waves, characteristic of the acute cor pulmonale.

Roentgen ray study of the acute cor pulmonale has not yet been adequately *carried out, in large part because of the very serious and transient nature of* the fulminating illness, but in rare cases cardiac dilatation has been noted. With acute pulmonary embolism the diaphragm on the affected side tends to be elevated but the infarction itself may not be evident for twenty-four hours or more, and in some cases with good collateral circulation pulmonary embolism is not followed by infarction.

In the acute cor pulmonale the pulse is usually rapid and regular the arterial pressure is low and the venous pressure is often high.

Pulmonary embolism either with or without the acute cor pulmonale, is often wrongly diagnosed or missed entirely It should always be thought of when there recur at intervals of days to weeks unexplained episodes of chest discomfort, dyspnea, tachycardia, fever or blood spitting. Frequently only one of these symptoms is present, although as a rule one finds an elevation of temperature, pulse rate, and respiratory rate together the latter two out of proportion to the height of the fever Pulmonary embolism will be discussed more fully in Chapter 28

Course and prognosis. The course and prognosis of the acute cor pulmonale are extremely variable. Many cases die quickly more often from the state of shock incidental to the pulmonary embolism than from right heart failure. In many cases the condition is probably very transient, lasting but a few hours at most and thus accounting for its neglect in the past or confusion with other conditions because of lack of time for study A few cases show the condition for several days prior to recovery or to death from another pulmonary embolus. Doubtless in many cases the acute cor pulmonale is but slight and can be recognized only by very careful study

Complications. The chief complications of the acute cor pulmonale are vasomotor shock which may abolish the cardiac dilatation, recurrent pulmonary embolism which is not uncommon and is likely to end fatally myocardial ischemia or actual infarction, particularly in cases with serious coronary artery disease already and congestive heart failure. *Massive pulmonary embolism with resulting strain on the right ventricle causing dilatation and failure may itself complicate chronic heart disease and produce a grave condition that not infrequently terminates fatally but the immediate significance of* which is often misunderstood this is particularly true of severe mitral stenosis and of hypertensive or coronary heart disease with congestive failure. The commonest complication of mitral stenosis and of congestive heart failure is pulmonary embolism and an occasional complication of acute myocardial infarction (from coronary thrombosis) during convalescence is pulmonary embolism, which has often been wrongly diagnosed as a new attack of coronary occlusion.

Treatment. Therapy of the acute cor pulmonale includes absolute rest with head elevated (unless a state of shock supervenes) morphine ¼ gr (0 015 gm) subcutaneously and oxygen inhalation (by tent) It is advisable to give digitalis in full dosage if the right heart fails digitoxin 0.5 mg intravenously or by mouth, repeated in 3 hours, and again if necessary or digoxin 0 8 mg intravenously repeated in 3 hours, or digitalis leaf in solution 0 5 gm intravenously repeated in 3 hours. Pulmonary embolectomy introduced many years ago (Trendelenburg, 1908) and carried out in a few cases proved to be an impracticable measure and, as a rule, unsuccessful because the emboli are so often multiple or split and because the operation itself is so hazardous. Papaverine hydrochloride has also been recommended for the treatment of acute cases in the dosage of 0 1 to 0 2 gm, but its use is in general disappointing.

It is even more important in treatment inasmuch as recovery is likely from the damage already done to search as soon as possible for the thrombosed vein in the leg which has been responsible for the massive pulmonary embolus which in turn has caused the acute cor pulmonale since life hangs in the balance from the threat of another and quite possibly fatal embolus The most careful physical examination may fail to reveal the thrombosed vein contrast (Diodrast) roentgen ray study may show it readily but it is also unreliable and may itself induce thrombosis (see Chapter 28) Ligation of the offending or threatening veins of one or of *both* legs, is often necessary to save lives. The use of heparin intravenously by constant drip though often helpful, is not always adequate and may delay essential surgery

Differential diagnosis. The three conditions that are very likely to be confused with the acute cor pulmonale are (1) acute coronary occlusion with rapid failure of the left ventricle and pulmonary vascular congestion secondary thereto, (2) congestive heart failure complicating heart disease and attended by râles at the lung bases which may also result from bilateral pulmonary infarcts (quite commonly occurring at both lung bases and not infrequently concealed behind congestive hydrothorax) and (3) pulmonary infection also attended by râles in the lungs and not uncommonly complicating heart disease. A careful history past and present, and the electrocardiogram usually distinguish these conditions, but the greatest difficulty arises when two or all three of them occur simultaneously in the same patient. There are two other acute thoracic episodes that, although much less common, need to be thought of and ruled out when pulmonary embolism is being diagnosed the first, namely spontaneous pneumothorax, is more frequent and easy to identify the second, *spontaneous mediastinal emphysema* a related condition, is rare and not always clear it is best diagnosed by the combination of substernal pain, a curious crunching sound over the heart in systole, roentgen ray evidence of air in the mediastinum, and sometimes an escape of air into the subcutaneous tissues of the neck (Hamman, 1939)

COR PULMONALE (PULMONARY HEART DISEASE)

Etiology *Cause* The cause of the condition called chronic pulmonary heart disease is chronically increased resistance in the pulmonary circulation, due commonly to the narrowing of its arterioles and capillary bed and not the result of left heart failure, mitral stenosis, or congenital heart disease. The *most pronounced and characteristic degree of the chronic cor pulmonale has* been that associated with silicosis, extensive pulmonary and pleural fibrosis, and the rare pulmonary endarteritis obliterans. In lesser degrees the chronic cor pulmonale may result from marked pulmonary emphysema, tracheal or bronchial stenosis, pulmonary collapse or in excessively rare cases in infancy failure of the alveoli to develop chronic inflammatory conditions of lung parenchyma, mechanical factors resulting from chest deformities, pulmonary arteriovenous communications (fistulae) congenital or acquired, and other intrathoracic conditions. Infrequently permanent and extensive obstruction of the blood flow in the major pulmonary arterial trunks by large fibrosed thrombi originating as pulmonary emboli, from the acute effects of which the patient has recovered, is the cause of the chronic cor pulmonale and is likely to be overlooked clinically Rarely pressure on and obstruction of the pulmonary artery by a syphilitic aortic aneurysm (Garvin and Siegel, 1939) may be to blame.

Primary endarteritis obliterans of the pulmonary arteries, noted first in several cases in the nineteenth century is generally of unknown cause, but in rare cases it has been ascribed to syphilis (Ayerza, 1901 Arrillaga, 1912) Because of the deep cyanosis that has been seen in a few cases of this type the patients have been sometimes called "black cardiacs," but undoubtedly the major part of the cyanosis in these black cardiacs is due to the primary pulmonary disease, which prevents the oxygenation of the blood, and not to the *secondary heart disease although, of course, right heart failure with resulting* systemic venous stasis accentuates the cyanosis (see Chapter 4) Clinically the effects on the heart of severe chronic pulmonary disease and of pulmonary endarteritis obliterans are much the same, and they will be discussed together

Age The heart disease that follows chronic pulmonary lesions occurs mostly in older persons. Of the twenty-one cases of White and Jones series, all but four were more than 50 years old, and thirteen were over 60 years of age In Scott s series of fifty autopsied cases (Scott and Garvin, 1941) thirty-five were over 50 years old and sixteen over 60. The age incidence of primary pulmonary endarteritis is younger the condition being found mostly in young and middle-aged men the youngest case that I have encountered was a boy 11 years old at death.

Sex With respect to the cor pulmonale males are much in the majority as might be expected in view of their well-known greater incidence of marked emphysema and pneumoconiosis (silicosis, anthracosis, asbestosis) Of 25 cases of chronic cor pulmonale of high degree found among 4 000 autopsies

at the Massachusetts General Hospital in the ten-year period of 1932 to 1942, 20 were male and only 5 were female (White, personal analysis in 1942) in Scott's series of 50 cases, 48 were male and only 2 were female.

Predisposing factors Severe climate, poverty malnutrition, and hereditary influences are factors which favor the occurrence of chronic pulmonary disease and thoracic deformities responsible for the chronic cor pulmonale, but one of the most common predisposing factors of all is pneumoconiosis (especially anthracosis and silicosis) an industrial disease among coal miners and stone workers. The coal or stone dust may saturate the lungs in a very few years to cause marked fibrosis and obliteration of many small arteries in the lungs, tuberculosis and pneumonia are the common causes of death in these cases but a few succumb to heart failure with improvement in industrial hygiene this hazard is lessening.

Pathology The chronic cor pulmonale or pulmonary heart disease consists primarily of enlargement of the right ventricle (Figure 100, page 508) and of the pulmonary artery and secondarily of enlargement of the right atrium The increase in size of the right ventricle is due at first to hypertrophy as in the case of the left ventricular enlargement in systemic hypertension, later as the heart fails, dilatation of the right ventricle appears, with relative tricuspid insufficiency and right atrial dilatation. The essential lesion is that of hypertrophy of the individual muscle cells of the right ventricle. Such changes as fibrosis, fatty degeneration, and fatty infiltration are associated with certain other conditions, namely coronary disease, anemia, and obesity Failure, when it comes, is attended by dilatation, due to muscular fatigue and not to degenerative changes unless there are complications. Endocarditis and pericarditis occur only as rare and incidental complications in pulmonary heart disease.

The right ventricle may be but slightly hypertrophied in the milder cases, adding but little to the heart weight, escaping clinical observation, and passing notice sometimes even at postmortem examination. Usually the enlargement is considerable and in rare cases it may be very great so that the right ventricle is as large as, or larger than, the left ventricle and the blunt apex of the heart is made up in large part by the right ventricle (see Figure 101 as an example of marked right ventricular enlargement)

The pulmonary artery and its branches may show areas of atheroma of varying number and size and some narrowing of the smaller arteries when the blood pressure in the pulmonary circulation is much elevated, which happens in some cases of chronic pulmonary disease as it does in chronic mitral stenosis. There is a different finding, however in the case of pulmonary endarteritis obliterans, the rarer pulmonary cause of the chronic cor pulmonale: here one finds an actual hyperplasia of varying degree of the endothelium of the smaller arteries and arterioles, in extreme cases almost a complete arterial obliteration. In a few cases the treponemata of syphilis are reported to have been found in these endothelial lesions, in most cases the cause is still unknown. The left ventricle in the case of chronic pulmonary disease is not

primarily affected. It may however as in mitral stenosis, be rather small than usual this finding has probably given rise to the erroneous idea th chronic pulmonary disease and emphysema always spare the heart and resu in cardiac hypoplasia.

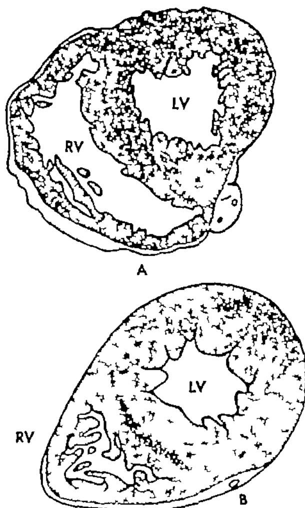


FIG. 100 Drawings showing cross sections of (*A*) a dilated cor pulmonale and of (*B*) a normal heart at a level two thirds of the distance from base to apex of the ventricles. These cross sections are of natural size. RV = right ventricle, LV = left ventricle.

In the case of silicosis two morphologic processes have been described which evoke vascular changes in the pulmonary circulation (1) direct encroachment on the vascular wall by nodules or nodular masses and (2) infiltration of the vascular wall by dust bearing and pigment-bearing granulation tissue (Geever 1947)

A very rare, bizarre finding as a cause of the chronic cor pulmonale in infancy is failure of the lung alveoli normally to open up at birth this results in

an extremely difficult bronchiolar respiration, endarteritis, marked enlargement of the right ventricle and early death within the first year (T B Mallory personal communication, 1942) A rare cause of subacute cor pulmonale is a gradual vascular obliteration by carcinomatous emboli (Mason, 1940)

Symptoms. The chronic cor pulmonale produces symptoms only when it begins to fail. Symptoms due to the chronic underlying pulmonary disease, namely dyspnea, cough, and weakness have often been wrongly interpreted as those of early failure in pulmonary heart disease this error was made in the first edition of this book. Actually symptoms of the heart failure are other than pulmonary and are due to congestion of liver gastrointestinal tract, and dependent parts of the body Pain, except in the congested liver and palpitation are rare and not characteristic.

Signs. There may be little or no evidence of the chronic cor pulmonale itself because it so often is concealed by the underlying pulmonary condition, but when the characteristic signs of marked chronic pulmonary fibrosis with emphysema are present, one may rest assured that the heart is at least somewhat affected although it may still be competent. A brief summary will first be given of the typical signs of advanced pulmonary fibrosis with emphysema and then the additional signs of cardiac involvement due to that condition.

The signs of marked pulmonary fibrosis with emphysema are (1) cyanosis of varying degree, often considerable and sometimes as intense as in the maladie bleue of congenital heart disease, (2) clubbing of the fingers and toes, (3) polycythemia, the red blood cells being increased to 6 or 7 millions per cubic millimeter (4) lowered oxygen saturation of the arterial blood, (5) restricted respiratory movements, with emphysematous or asthmatic breathing (expiration prolonged and forceful) (6) frequent, scattered, squeaking or groaning pulmonary rales, (7) low position of diaphragm with restricted respiratory movements very evident fluoroscopically (8) abnormally thickset or barrel-shaped chest, and (9) low vital capacity Most of these signs are also found in the cyanotic type of congenital heart disease and also, except for the constant cyanosis and rales, in long-time residents at very high altitudes (over 12,000 feet or 4 000 meters)

The cardiac signs are those due to enlargement of the right ventricle and to a complicating failure when it appears. Cardiac arrhythmia is uncommonly found. There is frequently a pulmonary systolic murmur and the pulmonary second sound is usually accentuated. The pulmonary arterial pressure is elevated to double or more the normal pressure (e.g. 50 or 60 mm mercury instead of 25) when tested by intracardiac catheterization. The systemic blood pressure is as a rule low at about 100 to 110 mm systolic and 70 to 80 mm diastolic.

The signs of failure are primarily those of failure of the right ventricle consisting of engorgement of the great veins, including the jugular veins, with the development of a jugular venous pulse in the upright and semiupright posture, liver enlargement and tenderness, ascites, and edema of the legs. Pulmonary signs are wholly those of the underlying pulmonary disease.

The right ventricular enlargement is often made out with much difficulty especially on physical examination. There are three reasons for this difficulty: In the first place, the right ventricle, being anteriorly placed, shows relatively less evidence of enlargement than does the left ventricle which increases downward and to the left, as well as backward; secondly the low level of the diaphragm so often found in chronic pulmonary disease, gives a deceptive, small cardiac appearance (a "drop" heart) even when the heart is somewhat enlarged and, thirdly the pulmonary emphysema, by making the thorax hyperresonant, often prevents satisfactory percussion for the determination of the heart borders and even interferes with auscultation. Thus, unless great care is exerted and electrocardiograph and roentgen ray are brought to one's assistance, the enlargement of the chronic cor pulmonale may easily escape notice; even with all this help the condition may be discovered only at postmortem examination. Electrocardiography shows right ventricular preponderance (Figure 101) unless there is also present left ventricular enlargement from some factor of strain (systemic hypertension, aortic valve disease, or myocardial infarction) in the same heart. The right ventricular preponderance pattern includes abnormal right axis deviation in the limb leads and especially higher peaks of the *R* waves in the precordial leads over the right ventricle (often with depressed or inverted *T* waves) and prominent *S* waves over the left ventricle. Roentgen ray study may or may not clearly show the right ventricular enlargement (Figure 102, see page 512); the view of the heart shadow in the anterior oblique positions is especially helpful in revealing the forward bulging of the right ventricle not made out in the anteroposterior position. Furthermore, fluoroscopy sometimes shows dynamic dilatation of the pulmonary artery which may be marked, especially in the case of pulmonary endarteritis obliterans. In this last-named condition the lung fields have been noted as abnormally clear but as a rule the lung fields are very abnormal due to the underlying pulmonary disease, silicosis, or chest deformity.

Course and prognosis. Pulmonary heart disease, or the chronic cor pulmonale, begins very gradually and insidiously, usually in the long course of severe chronic bronchitis and emphysema or silicosis, and years may elapse after it has been found before failure becomes marked. Its course and prognosis are so bound up with those of the pulmonary condition that the heart trouble must always be considered with the lung disease. Pulmonary infections, especially pneumonia and phthisis, have in the past, usually caused death in these cases, but many years of a careful life of moderate activity may elapse before death comes. It is probable that the limitations enforced by the pulmonary trouble protect the heart from excessive fatigue. Death from congestive heart failure in such patients occurs rarely.

The prognosis of cases with pulmonary endarteritis obliterans is less favorable than that of cases with chronic pulmonary fibrosis, death coming from cardiac failure in the course of months to a few years at best after cyanosis has become apparent.

Complications. The two important complications, heart failure, either right

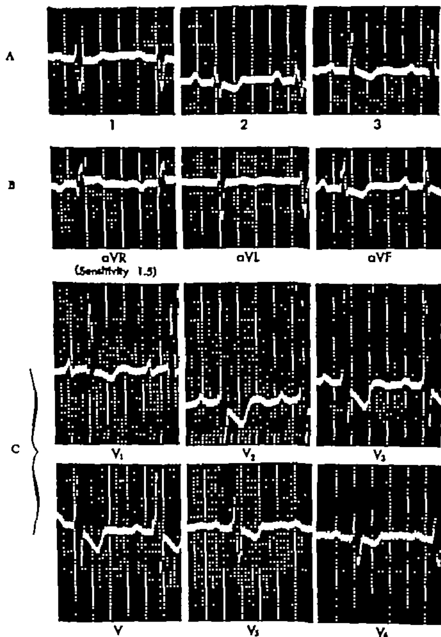


FIG. 101 Electrocardiogram in a case of chronic cor pulmonale, male, age 30. (*A*) Bipolar limb leads 1, 2, and 3. (*B*) unipolar limb leads, aVR, aVL, and aVF. (*C*) all precordial leads, V to V inclusive. Note the marked right axis deviation in the limb leads and the very high *R* and inverted *T* waves in the precordial leads V to V over the right ventricle. Time = 0.04 and 0.20 second, amplitude 1.5 mm = 0.15 mv





FIG. 102. Roentgenograms in two cases of the chronic cor pulmonale due to pulmonary endarteritis obliterans and pulmonary fibrosis. (*A*) Roentgenogram showing increased heart (right ventricular) size and prominence of pulmonary artery. Boy age 10 who showed at autopsy year later very extensive pulmonary endarteritis obliterans of unknown cause. (*B*) Roentgenogram showing extensive pulmonary fibrosis and chronic cor pulmonale in H.S.G male age 49

sided or incidentally left-sided, and respiratory infections, have been discussed above. Other types of heart disease may be associated with the chronic cor pulmonale but only one, coronary heart disease, occurs with much frequency Coronary heart disease is present in about half the cases, probably because of the advanced age of the majority of the patients.

Treatment. The treatment of pulmonary heart disease consists in the therapy both of heart failure when present and of the pulmonary disease itself but much more so of the latter since heart failure is rare in these patients. The usual therapy of congestive failure, if clearly present as shown by engorged liver leg edema, and increased jugular pulse, should be carried out (but not for dyspnea or cyanosis per se) rest in bed, digitalis, diuretics, and symptomatic treatment, as needed. Oxygen inhalation may prove to be especially helpful because of the pulmonary disease.

A therapeutic test with digitalis in cases of chronic bronchitis and emphysema is often helpful, since heart weakness is easily masked by the pulmonary condition. When signs of right heart weakness are thereby decreased we have confirmatory evidence of the chronic cor pulmonale or of a secondary effect of coincidental left heart weakness, careful differentiation between these two fundamental conditions is essential and will be discussed at length in Part IV When, however dyspnea, cough, and cyanosis are appreciably decreased by saturation of the patient with digitalis we have evidence only of left ventricular weakness and failure and not of the chronic cor pulmonale. If in either case there has been benefit by digitalis, its administration should thereafter constantly be maintained by daily rations of the drug, and in cases of considerable right ventricular enlargement it is conceivable that regular rations of digitalis may help to retard the onset of heart failure in the first place.

Care to avoid respiratory infections, the treatment of the pulmonary condition already present, the avoidance of fatigue, residence in a more favorable (drier) climate and not at high altitudes, and symptomatic therapy especially the use of penicillin and oxygen as needed, will have a favorable influence on the course of pulmonary heart disease.

If syphilis is found present in rare cases of pulmonary endarteritis obliterans specific therapy should be instituted with care, as outlined for syphilitic aortitis in Chapter 16.

Advances in thoracic surgery in the correction of chest deformities and pulmonary disease afford some hope for the future eradication of underlying causes of the chronic cor pulmonale in a few cases, even perhaps the removal of extensive thrombi, more or less organized, from the pulmonary artery itself or from its chief branches in rare subacute or chronic cases when the responsible factor is obviously embolic thrombosis.

Differential diagnosis. There are two conditions from which it is often difficult to distinguish pulmonary heart disease (1) the pulmonary disease itself, and (2) congenital heart disease without characteristic murmurs (as in some cases of the tetralogy of Fallot, which consists of pulmonary stenosis,

interventricular septal defect, dextroposition of the aorta, and enlarged right ventricle) The presence of the emphysema, the absence of any history of heart trouble or cyanosis in youth, and the lesser degree of abnormality of the heart as determined by various methods of examination help to distinguish the chronic cor pulmonale from congenital heart disease, though it is to be noted that pulmonary arteriolar disease and emphysema may themselves be important complications of congenital heart disease (the maladie bleue) The finding of right ventricular enlargement by roentgen ray and electrocardiogram, the favorable response to the therapeutic test with digitalis, and indeed the very presence of marked chronic emphysema, point to pulmonary heart disease as a complication of emphysema. Pulmonary endarteritis obliterans is found in younger individuals without pulmonary disease itself, is sometimes attended by intense cyanosis (the "black cardiacs") and has usually a rapid downhill course. Mitral stenosis may in rare cases simulate pulmonary heart disease when the pulmonary vascular congestion is considerable and the right heart begins to fail, but careful study particularly the finding of the characteristic mitral diastolic murmur should clearly distinguish the two conditions.

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SEE ALSO REFERENCES UNDER CHAPTERS 3 SYMPTOMS 4 SIGNS AND 28 VASCULAR DISEASE

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CHAPTER 21

CORONARY HEART DISEASE
ANGINA PECTORIS
CORONARY THROMBOSIS AND MYOCARDIAL INFARCTION

Introduction. For convenience and consistency a simple rearrangement has been introduced into this new edition whereby the former Chapter 31 on Coronary Insufficiency Including the Symptom Angina Pectoris, has been for the most part incorporated into the present chapter where it best belongs, thus omitting considerable repetition and saving space, and the short appendix on Atherosclerosis has been transferred appropriately to Chapters 26 and 28.

This chapter is one of the most important in the book and demands at the outset the consideration of basic definitions, nomenclature, and arrangement, too often neglected or confused in the rapidly growing literature on the subject. In the first place "coronary disease" is not heart disease though it is often loosely and inaccurately designated as such. Strictly it does not even mean coronary artery disease since coronary veins form an important part of the coronary circulation; common usage, however, and the fact that in the present state of our knowledge the coronary veins are not the site of any serious pathologic process justify the use of the term as synonymous with coronary arterial disease. Also, since practically the totality of coronary arterial disease is atherosclerotic in type, coronary atherosclerosis is implied when the term *coronary disease* is used without other qualification. The designations "coronary insufficiency" and "coronary failure," usually attended by the symptom angina pectoris and often leading to myocardial infarction, are not strictly synonymous with coronary disease since other conditions such as syphilitic aortitis, with a blocking of the coronary circulation at its origin, may be the cause, and since coronary disease, even extensive in degree, may be present without insufficiency of blood supply to the heart muscle.

The terms "coronary occlusion" and "coronary thrombosis" have been loosely used to indicate myocardial infarction, but there should be a correction

1 I am grateful to Sir John Parkinson for his helpful advice in this respect.

of this common error To be sure, myocardial infarction often results from acute coronary thrombosis or occlusion, but the two designations should not be employed synonymously· myocardial infarction may occur without actual complete coronary arterial thrombosis or occlusion, and coronary occlusion may occur without myocardial infarction, if the process is slow in development or (and) the collateral circulation is adequate. What has usually been meant clinically by the diagnosis of coronary thrombosis as an acute illness is myocardial infarction. The terms "coronary occlusion and "coronary thrombosis" are not strictly synonymous either although as acute processes they can be so considered for practical purposes, old calcareous occlusions of the coronary arteries may exist with never any symptoms therefrom and not even proof of past thrombosis.

Finally the term "coronary heart disease" continues to be to my mind the best designation for the various effects of coronary arterial disease on the heart deleterious enough to cause symptoms or signs or postmortem evidence of more than trivial damage to the heart itself chiefly of course to the heart muscle. Thus, myocardial ischemia with angina pectoris or electrocardiographic abnormalities due to coronary disease, acute myocardial infarction, and old scars of similar origin are all included under this heading In the first two editions of this book acute coronary thrombosis with myocardial infarction was not considered, as was the general custom in those days, as a separate entity in a chapter by itself since it is but a phase of coronary heart disease. New knowledge has confirmed the soundness of continuing this procedure in the third and fourth editions.

Historical. The earliest correlation of coronary disease with serious illness was made by Bonetus in 1700 in the second edition of his *Sepulchretum* when he described the case of a fat middle-aged poet who succumbed in a few minutes after the onset of "distress in breathing" (which may have been angina pectoris) and who showed at autopsy calcified coronary vessels which were almost, if not completely occluded. Morgagni in 1761 was, however, unaware of the symptomatology of coronary disease and seven years later (1768) Heberden (quoted on page 538 of this chapter) was unaware that angina pectoris which he described so well was due to heart trouble. It was Jenner a few years later (in 1772 as quoted by Parry 1799) who made that discovery Fothergill (1776) and Black (1794) published case reports of angina pectoris with ossified coronary arteries" and the former also described myocardial scars.

During the nineteenth century and until our own generation (Herrick, 1912) astonishingly little advance was made in the clinical recognition of coronary heart disease, despite the important contributions, mostly anatomic, of Weigert (1880) Cohnheim (1881) Ziegler (1881) Huber (1882) Leyden (1884) and Marie (1896)

The following quotation from Herrick s classical paper presents the earliest complete clinical description of sudden coronary occlusion Herrick recog-

nized even at the beginning that the clinical picture is often complex and variable, a fact that has been re-emphasized of late.

Herrick, J B. "Clinical Features of Sudden Obstruction of the Coronary Arteries. *JAMA* 1912, LIX, 2015

"Obstruction of a coronary artery or of any of its large branches has long been regarded as a serious accident. Several events contributed toward the prevalence of the view that this condition was almost always suddenly fatal.

"But there are reasons for believing that even large branches of the coronary arteries may be occluded—at time acutely occluded—without resulting death, at least without death in the immediate future. Even the main trunk may at times be obstructed and the patient live. It is the object of this paper to present a few facts along this line, and particularly to describe some of the clinical manifestations of sudden yet not immediately fatal cases of coronary obstruction.

"The influence of the vessels of Thebesius is also not to be overlooked in this connection, compensatory circulation through these accessory channels may be of considerable importance in nourishing areas of heart muscle poorly supplied by sclerotic or obstructed arteries.

"The clinical manifestations of coronary obstruction will evidently vary greatly depending on the size, location, and number of vessels occluded. No simple picture of the condition can, therefore, be drawn. All attempts at dividing these clinical manifestations into groups must be artificial and more or less imperfect. Yet such an attempt is not without value, as it enables one the better to understand the gravity of an obstructive accident, to differentiate it from other conditions presenting somewhat similar symptoms, and to employ a more rational therapy that may to a slight extent at least, be more efficient.

A study of cases of this type shows that nearly all are in men past the middle period of life. Previous attacks of angina have generally been experienced, though as shown by my first case, the fatal thrombosis may bring on the first seizure. The seizure is described by patients who have had previous experience with angina as of unusual severity and the pain persists much longer In some instances there has been no definite radiation of the pain, as to the neck or left arm, though this may have been a feature of other anginal attacks, and the pain, as in these two cases, may be referred to the lower sternal region or definitely to the upper abdomen. Cases with little or no pain have been described. Nausea and vomiting, with belching of gas, are common. There may be tympany Ashy countenance, cold sweat, and feeble pulse complete the picture of collapse. The attention f the patient and the physician as well may therefore, be strongly focused on the abdomen, and some serious abdominal accident be regarded as the cause of the sudden pain, nausea, collapse.

"Cohnheim found that in dogs the pulse after obstruction was slow This may be seen in the thrombotic obstruction of disease in man. In Hammer's case (1878) the pulse dropped from 80 to 8 per minute, the patient living thirty hours from the onset of the symptoms that marked the closure of the right coronary opening. A rapid pulse is frequently seen, however The pulse may be irregular A striking feature has been its weakness. Blood pressure is low The heart tones have been feeble—in fact, often startlingly feeble.

"Dyspnea and cyanosis have been variable, at times much less than one would expect from the character of the accident and the quality of the heart's action. Râles, dry and moist, have been present in many cases.

"General weakness has been marked in some cases, in others not.

"The occurrence of serofibrinous exudate over the area of myocardial softening, with roughening of the pericardium, has been noted in several instances. This may explain a later precordial distress, as in Case 1 A fine pericardial friction, therefore, occurring several hours or a few days after the initial pain, may be confirmatory evidence of coronary obstruction.

"Death may be caused by rupture, by sudden asystole, or by gradual giving out of the weakened heart muscle.

"Emphasis ought to be laid on the resemblance of some of these cases to surgical accidents.

If these cases are recognized, the importance of absolute rest in bed for several days is clear It would also seem to be far wiser to use digitalis, strophanthus, or their congeners than to follow the routine practice of giving nitroglycerine or allied drugs.

Incidence. Extensive coronary arteriosclerosis is not only a very frequent and important cause of heart trouble near the end of the life cycle, but it also cripples and kills often in the prime of life and sometimes even in youth. It is problematic whether the coronary sclerosis of senile life can ever be controlled, but it is to be hoped and expected that some progress can be made in the prevention of such disease in persons who have not reached old age.

Coronary atheroma and sclerosis of slight to moderate degree are doubtless but part and parcel of the process of growing old. Not only is it difficult, indeed impossible, in the present stage of our knowledge to recognize the limits of the normal range, anatomically as well as clinically at any particular age, but even when the coronary arteries are markedly involved the heart itself may remain both structurally and functionally essentially normal. This is a very important but inadequately recognized fact. Of a series of 1 000 consecutive postmortem examinations, 371 cases (37 1 per cent) showed macroscopic coronary disease, while of these 371 cases only 238 (64 per cent) showed any definite myocardial lesions (fatty change alone in 48 of them, and fibrosis in the remaining 190) (Allan, 1928) It is, furthermore, to be observed that limitation of blood supply to the heart by narrowed coronary vessels may limit cardiac action and reserve without actually causing structural lesions.

Coronary sclerosis as a cause of heart disease varies somewhat in its relative incidence in different parts of the world largely according to the frequency of such other causes as rheumatic heart disease, hypertension, and syphilitic aortitis. It is of interest that although heart disease has been on the increase since 1930, this has largely been due to a rise in the incidence of coronary heart disease in contrast to other types of heart disease (Figure 103) In New England 37 per cent of a series of 2,314 patients with organic heart disease were diagnosed as having some grade of coronary heart disease in about half of them uncomplicated and in the other half complicating other types of

heart disease, mostly the hypertensive type (White and Jones, 1928) A recent survey of 3 000 cardiac patients in New England showed a considerable increase of the relative incidence of coronary heart disease, up to 48.5 per cent (White, 1951)

In Clawson's series (1941) of 4 678 cardiac deaths among 30,265 autopsies there were 1,215 cases of coronary heart disease (30 per cent of the cardiac cases) three quarters of which were also hypertensive. Statistics at present are not truly comparable, for sometimes only those cases are recorded as

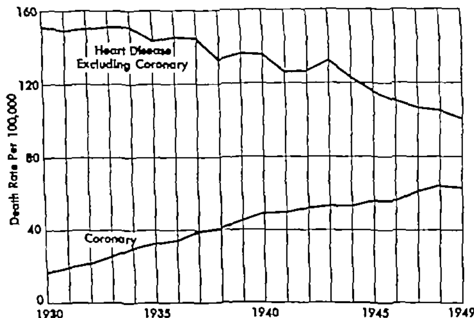


FIG. 103 Annual age-adjusted death rates of insured individuals from diseases of the coronary arteries as compared with other chronic diseases of the heart. Ages 1 to 74 years. Metropolitan Life Insurance Company 1930–1949 (Statistical Bulletin, Metropolitan Life Insurance Company New York City [January] 1950, XXXI, 11)

coronary heart disease in which the coronary involvement is the primary cause of disability or death, while sometimes all cases are so tabulated that show any suggestion of coronary involvement whatsoever We need many more studies than we possess at present to determine to what extent coronary disease, including coronary thrombosis, has been increasing, if at all, in the present generation. Two representative studies of the few that are available are as follows Meakins and Eakin (1932) found that the percentage of incidence of coronary thrombosis with occlusion (slightly less than 1 per cent) among the autopsies at the Royal Victoria Hospital in Montreal in the five-year period from 1926 to 1930 inclusive was actually less than that from 1896 to 1900 inclusive and Levy Bruenn, and Kurtz (1934) reported that the autopsy diagnosis of coronary disease at the Presbyterian Hospital in New York City

increased from 17 8 per cent in the decade from 1910 to 1920 to but 30.4 per cent in the next decade while the cases with the clinical diagnosis of coronary disease jumped from 7 to 454 The autopsy diagnosis of coronary thrombosis and of myocardial infarction at the Massachusetts General Hospital rose rapidly in incidence among the total autopsies from rare cases in the middle 1920s to 13 to 14 per cent in 1940 and 1941 probably due in considerable part to more careful search by the pathologists (Wang, et al., 1948) It may be that coronary heart disease or its symptoms, in particular angina pectoris, are more common in this day and age at any rate it is certain that the diagnosis is much more often made during life. Even young people with coronary heart disease are now being reported quite often, the largest series being 866 in number 450 of whom were confirmed at autopsy aged 18 to 39 years, in U S.A. military service (Yater et al., 1948)

Etiology *Cause* The reduction of the blood supply to the myocardium explains the deleterious effect of coronary disease on the heart. This blood supply is reduced by the narrowing or obstruction of the coronary arteries locally or generally: a slight degree of abnormality of the coronary arteries may exist, however without restriction of blood flow Moreover other causes exist for a poor blood supply to the myocardium even when the coronary arteries themselves are normal severe anemia, marked aortic stenosis or regurgitation, extreme bradycardia, extreme tachycardia, marked temporary hypotension (as with vasodilatation in "surgical shock") and blocking of the mouths of the coronary arteries by large vegetations on the aortic valve or by syphilitic aortitis.

Coronary disease may be of various types. In the normal evolution of the coronary circulation, simple thickening of the elastic-hyperplastic layer of the intima *may occur so that, in contrast to other arteries of the same size,* the intima may exceed the media in thickness, doubtless due to the fact that these are the smallest vessels receiving blood under a high head of pressure (Wolkoff, 1929) only if this change is marked is it to be considered as pathologic. A fibrotic thickening may also develop, especially in certain areas. Dock (1946) reported the findings of a thicker coronary wall and relatively narrower lumen normally in the male than in the female infant.

In the great majority of cases of coronary artery disease ordinary *atheroma* (*ἀθήρη*, meal or porridge) is to blame: this consists of softening, the precursor of arteriosclerosis, with yellowish fatty (cholesterol) areas in the endarterium. Fibrosis, thickening, so-called cholesterol abscesses, and calcification ensue and the arteries may become brittle the "abscesses" sometimes break or give rise to ulcerations whereby thrombi may form. Hemorrhages from the rupture of minute vessels (vasa vasorum) in the vascularized atherosclerotic walls of the diseased coronary arteries are thought also to favor or to precipitate coronary thrombosis (Paterson, 1936, 1941) A tendency to either thrombosis on the one hand or to hemorrhage on the other as characteristic of cases of *acute coronary occlusion has been suggested in the past, but not confirmed.* Reaction to atheroma is both fibrosis and especially in older decades, calcifi-

cation and the formation of cholesterol abscesses (Leary 1935) See Figures 104 and 105

The cause of atheroma of the coronary arteries, as well as that of arteriosclerosis in general, is still unknown. Faulty cholesterol metabolism, local



FIG. 104 Microphotographs of coronary arteries with moderate atherosclerosis. (*A*) High power magnification of lipoid cells underlying the endothelium and overlying collagenous bands of fibrous tissue (scarring from previous deposits of the sort) in coronary artery of man of 54 years. X 280. (*B*) Microphotograph of coronary arteries in youthful case of extensive coronary atherosclerosis. X 30 times. Man, age 26, collapsed while removing a wheel from a automobile and died in few minutes. Note the almost complete obstruction of the descending branch of the left coronary artery by the extensive intimal fibrosis with necrosis i the deepest layer (crescentic in shape) just overlying the media, and the blocking of the small remaining lumen by fresh antemortem lot (stained black and roughly U-shaped) (Kindness of Dr Timothy Leary Boston City Hospital, Boston.)

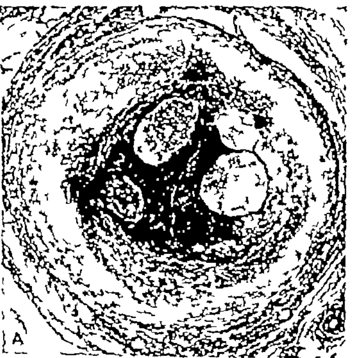




FIG. 103 Microphotographs of cross sections of coronary arteries in two cases of extensive coronary atherosclerosis showing later developments. X 30 times. (*A*) Man, age 53 who died suddenly at railroad station; he had had no illness and had worked continuously. Note almost complete obliteration of anterior descending branch of the left coronary artery with recanalization of an organizing thrombus in the old lumen. There is one new artery at the left and three veins above and to the right. (*B*) Man, age 62, found dead the day after strenuous work. Note the markedly fibrosed lumen of the anterior descending branch of the left coronary artery with four so-called atheromatous abscesses (atherocheumata) one discharging into the small oval lumen of the artery in which there is fresh antemortem thrombus. (Kindness of Dr Timothy Leary Boston City Hospital, Boston.)

arterial strain or overwork, hypertension, infection, allergy endocrinopathy and heredity are among the many factors suggested, but none has been proved or even consistently found. The frequent finding of a high blood cholesterol content in fasting cases of coronary heart disease, especially in the young patients under 40, along with a low basal metabolic rate, is in favor of a disturbance of fat metabolism, at least as one factor The suggestion of local overwork or strain is supported in the case of coronary atheroma by the finding that it is most common at the bend of the descending branch of the left coronary artery just below its mouth, and that serious coronary sclerosis relatively is more common in hypertensive individuals than in persons with normal blood pressure, the hypertension antedating any evidence of coronary disease, the frequency of coronary disease in myxedema and diabetes supports the idea of a factor of disturbed fat metabolism secondary to endocrinopathy and the factor of heredity is supported by the frequent finding of several members of a single family with serious coronary sclerosis. The combination of several etiologic factors is plausible.

An interesting presentation by Moreton (1948) of a possible mechanism based on the physiochemical introduction of coarse particulate matter containing fat (large lipid molecules) into the coronary artery wall where it acts as a foreign body illustrates a current viewpoint.

Considerable research is now in progress in an attempt to determine the responsibility of blood cholesterol and other lipids in the genesis of serious coronary atherosclerosis. Three varied types of investigation may be cited as examples of such research.

1 *Chemical.* An investigation of 100 persons (97 males and 3 females) who had acute coronary occlusion before the age of 40 years (Gertler and Garn and associates, 1950) have shown that more significant than the total cholesterol content of the blood, which was found to be elevated in most cases, was the ratio of such cholesterol to other phospholipids this was considerably higher than normal. Incidentally the blood uric acid was also found to be on the high side and this figure added to the other two in the form of a quotient has proved of considerable interest.

In keeping with this chemical study Barr (1951) has found in another chemical study of the blood fractions in atherosclerotic cases a higher ratio than normal of *beta* lipoprotein, which contains a larger amount of cholesterol in relation to phospholipids, to *alpha* lipoprotein, which contains much less cholesterol in relation to phospholipids.

2. *Physical.* Research on the blood lipoproteins by the use of the ultra centrifuge has also proved to be of special interest. Gofman, et al. (1950) found appreciably more of a light molecule of cholesterol-protein floated at a so-called SF 10 to 20 level in patients after recovery from acute myocardial infarction than in the case of normal controls, for example, 95 per cent in males and 100 per cent in females as compared to 60 and 45 per cent respectively at the age of 40 to 50 years.

3 *Tissue culture* Finally Simms (1948) has tested the amount of lip-

fanogens (precursors of visible fat) and of an inhibiting enzyme called antilipfanogen in the blood of normal and diseased individuals by determining the amount of fat taken up from the blood by tissue cultures. He has found that the ratio of antilipfanogen to lipfanogen, which is 1 0 in normal individuals, is much reduced in cases of nephrosis and diabetes and moderately reduced in patients with coronary heart disease.

A comparison of the findings of these three different technics, chemical, physical and by tissue culture, is in progress.

It is of interest to point out that the foods which contain maximum amounts of cholesterol, in order of content per average serving (not per weight) are brains, liver sweetbread scallops, oysters, eggs, lobster crabs, beef veal, pork, cheese, etc. By weight, eggs are second after brain.

On the other hand, it is also current opinion that the cholesterol that is deposited in the coronary artery wall may be produced in large part within the body itself that is, that it may be of endogenous origin. It conceivably may be both. It seems very likely that the total caloric value of the diet may be more important than the food elements themselves inasmuch as cholesterol may quite possibly be produced richly on a solely carbohydrate diet if hearty enough (witness the cow) if an inadequate or barely adequate diet (in calories) is given it is not so likely that cholesterol in large amount will be deposited in the coronary arterial intima, whatever the food ingested may consist of but that an excess diet with gain in weight may have such an effect, more readily (?) if there is rich cholesterol intake. Here, however we are dealing only with conjectures.

A different and rare type of coronary disease is that due to syphilis, here the media is primarily involved but later the intima too

Still another type of coronary disease, and one that is relatively infrequent, is that due to *rheumatic* or *other nonsyphilitic infection*. The intima and media are involved and there may even result aneurysmal dilatation (mycotic aneurysms)

Endarteritis obliterans is a very rare cause of coronary artery disease it is most often only a complication, being found in other vessels than the coronaries, mostly in the legs. It is itself of unknown origin, but the excessive use of tobacco has been suggested as an etiologic factor Related to this and of obscure origin is an extensive disease of the whole coronary artery wall in infants (Stryker 1946 Menten and Fetterman, 1948) *Periarteritis nodosa* may involve the coronary arteries at any age and has been noted to cause coronary thrombosis and myocardial infarction at even the early age of 1 year (Pickard, et al., 1947)

The coronary arteries, healthy or relatively healthy themselves, may rarely be blocked by *emboli* even of air so that death or cardiac infarction may result, or they may be more or less occluded at their mouths by syphilitic aortitis or by aortic valve vegetations in bacterial endocarditis. The pressure of tumors and perhaps even of pericardial fluid and constricting adhesions may interfere with the coronary blood flow

Trauma of the coronary arteries has been infrequently encountered as the result of pericardial paracentesis, stab and gunshot wounds, and unusual accidents. Hemopericardium and death from tamponade generally follow such trauma.

Rupture of a coronary artery may not only follow trauma but is a rare spontaneous occurrence as *the result of a dissecting aneurysm* extending from the aorta or limited to the coronary artery itself as a sequel to coronary thrombosis. Coronary aneurysms themselves are rare they may be congenital, mycotic, embolic, syphilitic, or arteriosclerotic—a series of 47 cases collected from the literature (Scott, 1948) showed 15 of the first, 12 of the second, 6 of the third, 6 of the fourth, while the remaining 8 were miscellaneous or unclassified.

Finally *congenital abnormalities* of the coronary arteries may very rarely account for trouble when the cardiac activity is such that a single vessel or some other restriction of blood supply is incapable of maintaining a normal blood flow to the myocardium, or when one of the coronary arteries arises from the pulmonary artery with resulting myocardial necrosis in the part of the heart supplied by this vessel. Such an anomaly the left coronary artery coming off the pulmonary artery was responsible for left ventricular myocardial necrosis, enlargement, and failure, and for attacks of distress on effort which were probably angina pectoris followed by early death in a four months old infant (Bland, White, and Garland, 1933) Coronary arteriovenous aneurysms or fistulae occur very rarely· I have encountered one such case in a boy of 9 years without disability who showed a continuous murmur at the right of the lower end of the sternum arousing a suspicion of coronary involvement which was found on surgical exploration (Paul, Sweet, and White, 1949)

Age The age of occurrence of coronary disease, and accordingly of myocardial changes due to coronary disease, varies from youth to extreme old age, but it naturally increases with years Statistical studies of the age incidence of coronary disease are likely to be misleading, because of the fact that slight atheromatous or atherosclerotic changes are frequently found in the coronary arteries on routine postmortem examination without their having any clinical importance whatsoever and hence not actually constituting disease from the clinical point of view and because a good many old persons with slight coronary insufficiency due to coronary disease do not trouble to seek medical advice, since they consider their condition to be simply a part of old age, as in fact it is. Several studies, in particular those by Wolkoff (1929) by Ehrich and his associates (1931) and by Leary (1935) have shown that atheromatous changes may be seen in the coronary arteries as early as the first decade when they may still be retrogressive. Atheroma and increase in thickness of the elastic-hyperplastic layer of the intima are found frequently in the anterior descending branch of the left coronary artery in the second decade and regularly in all cases over forty years of age; such changes are found later by about two decades, in the right coronary artery and other large branches. The age groups of 864 cases of coronary heart disease, diagnosed clinically

in New England (White and Jones, 1928) as compared with 1,346 recent cases (White, 1951) have been reported as follows

Table 9

AGE GROUPING OF CASES OF CORONARY HEART DISEASE

		Group I 864 Cases Reported in 1928 Percentage		*Group I 1,346 Cases Reported in 1951* Percentage	
Clinical coronary heart disease	Under 40 years of age	0.2		3.8	
	40 to 50 years of age	6.1		12.3	
	50 to 60 years of age	22.7	93.7	26.5	83.9
	60 to 70 years of age	44.1		33.1	
	Over 70 years of age	26.9		24.3	

This age grouping represents a cross section of the cases as they were seen by us the ages at onset of the disease would average a few years earlier as noted below

A series of 497 cases of angina pectoris gave the following age grouping at the onset of their disease (White, Bland, and Miskall, 1943)

Angina pectoris (age at onset)	30 years of age and under	4 cases,	0.8 per cent
	31 to 40 years of age	16 cases,	3.2 per cent
	41 to 50 years of age	106 cases,	21.4 per cent
	51 to 60 years of age	206 cases,	41.4 per cent
	61 to 70 years of age	131 cases,	26.4 per cent
	71 to 80 years of age	34 cases,	6.8 per cent
	Over 80 years of age	0 cases,	0 per cent

Our youngest case was 20 years old, our oldest was 80 the average age at onset was 56.5 years

The age incidence of coronary thrombosis with cardiac infarction diagnosed clinically is much the same as that of angina pectoris. The age groups of 461 cases analyzed by Bland and White (unpublished data, 1936) are as follows.

Clinical coronary thrombosis with myocardial infarction (age at onset)	Below 30 years of age	3 cases,	0.7 per cent
	30 to 40 years of age	16 cases,	3.5 per cent
	40 to 50 years of age	80 cases,	17.4 per cent
	50 to 60 years of age	169 cases,	36.6 per cent
	60 to 70 years of age	142 cases,	30.8 per cent
	70 to 80 years of age	47 cases,	10.2 per cent
	Over 80 years of age	4 cases,	0.9 per cent

Our youngest case was 22 years old, our oldest 81 the average age at onset of the entire series of 461 cases was 56.2 years. Since the analysis of this series, we have encountered in another series, that of 100 cases under the age of 40, six patients, all men, under the age of 30 (Gertler et al., 1950) I have seen still a few other patients under 30 years old, the youngest was a 22 year old soldier with xanthomatosis. Yater and his associates have reported 450 cases of men in military service who had fatal coronary heart disease as proved at autopsy between the ages of 18 and 39 years (Yater et al., 1948) The youngest cases of atheromatous coronary thrombosis on record have been

a lad aged 12 years with diabetes (Shivelhood, 1948) a girl aged 16 (Mac Dougall, 1949) a boy 18 years old (Jamison and Hauser 1925) and a young woman of 19 (Evans and Graybiel, 1948) One other case of progeria, male aged 7½ died of coronary occlusion at the Massachusetts General Hospital (Talbot, et al. 1945)

And now very recently (1949) Gertler and Garn of our Massachusetts General Hospital coronary research group, through the kindness of Drs. J B Hamilton and C. V Hawke, have studied a large group of eunuchs and found among them a strikingly low incidence of coronary heart disease, even in the older cases, and also a very low blood cholesterol content.

Coronary embolism, though rare, may occur at any age, even in youth. Two cases of cardiac infarction so caused, under the age of 30 years, have been reported by Parkinson and Bedford (1928) even in infancy cardiac infarction due to infectious embolism is on record (Schaps, 1905) There are also two reports of paradoxical coronary embolism from a femoral vein thrombus in a man aged 35 years and in a woman aged 47 both without coronary disease (Saphir 1933 Jacobi, et al., 1934)

Sex The male sex is more often affected, and to a more serious degree, by coronary heart disease than is the female. In a series of 200 clinical cases of cardiac infarction (Bland and White, 1941) 168 (84 per cent) were male and 32 (16 per cent) were female, while in a series of 83 postmortem cases of the same condition reported by Parkinson and Bedford (1928) 72 were male and 11 were female. The ratio of males to females in Clawson s autopsied series of 1,215 cases of coronary heart disease (1941) was 4.2 to 1 The most interesting and highly significant ratio of all has been in two separate groups of 100 patients each under the age of 40 years with coronary heart disease, with or without myocardial infarction, the first group reported by Glendy Levine, and White in 1937 and the second group under recent study by our research team at the Massachusetts General Hospital there were 96 males and only 4 females in the first group and 97 males and 3 females in the second. These findings would appear to be of great significance in the consideration of the etiology of coronary heart disease and demand further analysis. *Why should the robust and apparently most masculine young male be particularly prone to this disease?* Is there a sex difference in the metabolism of fat or in its deposition? Does the greater thickness of the coronary artery wall in the male than in the female infant reported by Dock (1946) and by Minkowski (1947) play a role? Is it a part of the law of the animal kingdom whereby the male is more vulnerable than the female with a shorter life span (Hamilton, 1948) by 4 or 5 years in the U.S.A. of recent years?

Other etiologic factors Race, temperament, social and economic status, and occupation appear to have but slight bearing on the incidence of coronary heart disease. At one time it was thought that coronary atherosclerosis was uncommon in the Negro, but now increasing evidence thereof has been adduced by more adequate studies, recent reports have been published by Hunter (1946) and Smith (1946) It is still stated that coronary thrombosis

is comparatively rare in the Chinese, but similarly further studies thereof are needed.

Certain symptoms associated with coronary disease, namely angina pectoris and the pain and prostration of acute coronary thrombosis, are more often found in sensitive, mentally overworked, and frequently robust or stout professional and business men than in other individuals. Whether coronary thrombosis is actually more common in such persons has not yet been shown, but one has the definite impression that it is less common in the lean laborer or farmer: further study of this important point is, however essential.

One of the most impressive clues in our studies to date is anthropologic: the majority of the young cases are not only male but mesomorphic (muscular type) there being no pure ectomorphs (very lean type) in the series, although there are mixtures of mesomorphy with ectomorphy and, more often, of mesomorphy with endomorphy (fat type with large abdomen) Does the muscular metabolism of the robust mesomorphic male play a role in the early development of serious coronary atherosclerosis? Especially so if he makes but little use of his muscles?

The effect of climate has not yet been adequately studied in relation to the incidence of coronary heart disease.

Alcohol, tobacco, tea, and coffee are probably without direct influence, except that in occasional individuals the symptom of coronary insufficiency namely angina pectoris, is precipitated or aggravated by excessive use of tobacco, while heavy indulgence in alcohol over many years may have a damping influence on the symptoms but not otherwise on the ill effects of coronary heart disease.

Heredity as already mentioned, does appear to exert a definite action. There may well be an inherited family coronary arterial tree in some families more branching and interlacing may occur than in others who are prone to develop coronary heart disease. This important point needs accurate evaluation. Probably however of more importance is the inheritance of body build, that is, of mesomorphy mentioned above, and of a metabolic fault whereby atheroma is favored. The hereditary predisposition to certain diseases which favor the occurrence of presenile coronary heart disease, namely diabetes mellitus, xanthomatosis, and hypertension, is certainly an important consideration. Hereditary hypercholesterolemia and familial xanthomatosis in a series of 35 families (172 members) and 29 individuals, with 40 per cent showing coronary heart disease, constituted an inherited incomplete dominant trait (Adlersberg and Parets, 1949) Familial liability to sudden coronary death was reported by Herapath and Perry in 1930 in the persons of a father aged 42 and of his three sons aged 43 31 30.

Pathology A discussion of coronary artery atherosclerosis itself and of other coronary artery diseases has been presented under the preceding section of Etiology and need not be repeated here.

The effect of coronary disease on the heart is extremely variable in degree and rapidity of involvement. There may be only ischemia without structural

change, there may be slight fatty degeneration, generalized or local, with a late sequela of slight fibrotic change, there may be extensive changes due to single or multiple infarctions, which are so gradual in development that the heart remains competent though with lowered reserve, the fibrosis occurring in limited small or large areas, or diffusely or there may be a suddenly developed myocardial infarct, small or large, fatal or outlived, involving one part or another of the left ventricle, rarely the right ventricle or both ventricles, and due to occlusion by thrombosis or embolism of one of the main coronary artery branches. The size of the infarct, the prognosis, the process of repair and the completeness of healing depend on several factors the size of the artery occluded, the rapidity of occlusion, the extent of either congenital or acquired anastomotic or collateral coronary circulation (and possibly also of other blood channels including the Thebesian circulation and extracardiac blood vessels in the pericardial attachments) and the effectiveness of treatment.

The major and by far the most important source of the collateral coronary circulation that so often rescues the myocardium from anoxia is undoubtedly the multitude of small anastomotic arterial branches themselves which gradually grow larger and more and more competent to supply the need through the years.

The Thebesian vessels are small channels opening into the heart chambers especially the ventricles, of varying numbers and size they connect directly with coronary capillaries and veins and by sinuses with the arterioles, and probably are the vestiges of the intertrabecular spaces of the primitive ventricle whereby blood was brought into contact with the cells of the myocardium before the development of an adequate coronary circulation. These Thebesian vessels are of uncertain function and value, but sometimes they and especially other blood sinuses which link up various parts of the coronary circulation may well be helpful when the regular channels of blood supply to the myocardium are obstructed, as in rare reported cases in which life continues for a while in spite of complete and chronic occlusion of both coronary arteries in such cases, however highly placed and anastomotic coronary arterial branches, proximal to the points of block, doubtless play the major role in maintaining the myocardial circulation. Compensatory circulation to the myocardium by way of extracardiac vessels developing over the pericardial attachments or adhesions, as from the bronchial arteries is probably sometimes available in addition to the blood supply via the Thebesian vessels and the myocardial blood sinuses, but adequate blood vessels of the sort would seem to be rare this idea has, however pointed to the possible value of artificially introducing blood supply from the outside and Beck and O'Shaughnessy have done this in man, the former using at first the pectoral muscle (1935) and the latter the omentum through the diaphragm (1937) work which still remains in the experimental stage and in which other technics are being tried (Beck, 1948)

The descending branch of the left coronary artery near its mouth is the place most commonly affected both by extensive sclerotic change and by

thrombosis When there is a sudden occlusion at this spot an infarct usually appears in the anterior wall of the left ventricle near the apex and often involves also the anterior and lower part of the interventricular septum (Figure 106A) This is the commonest site of cardiac infarction, and the descending branch of the left coronary artery has as a result of its lethal role been called the "artery of sudden death." The preponderance of involvement of this artery and of this part of the left ventricle is not, however so great as used to be

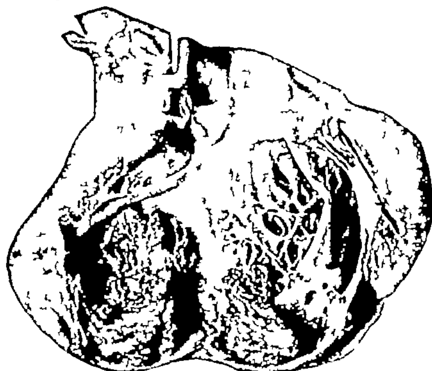


FIG. 106A. Photograph showing a large fibrosed cardiac i farct about four months old in the anterior and apical part of the left ventricle involving the septum and the base of the papillary muscles, and resulting from thrombosis of the descending branch of the left coronary artery with mural thrombus in the cardiac aneurysm resulting from the infarct. This lesion was found in a man 68 years old.

believed it is only slightly in the lead. The reason for the erroneous idea of some years ago was that a careful enough search was not always made for old scars at other sites and also because there was more often recovery from infarcts in other sites and patients leaving the hospitals were lost to view

The second most likely spot for infarction is the posterior wall of the left ventricle near the base behind the posterior cusp of the mitral valve, due usually to occlusion of the right coronary artery or of the circumflex branch of the left (Figure 106B)

The relative frequency of thrombosis of the three larger coronary arterial trunks in a series of 49 cases of myocardial infarction found in 1 000 consecutive autopsies at the Mayo Clinic was as follows anterior descending branch

of the left in 28 cases, right coronary 20 cases, and circumflex branch of the left 17 cases (Barnes and Ball, 1932) In that series of cases the infarct involved the apex and anterior portion of the left ventricle in 25 cases and the posterior basal portion of the left ventricle in 21 cases, while the remaining 3 hearts showed two infarcts, one at the apex and one at the base In another series of 34 cases (Saphir et al., 1935) both coronary arteries were involved in all of the cases but the more severe lesions were found in the anterior descending branch of the left. There was involvement of at least two coronary



FIG. 106B. Photograph showing a small fibrosed cardiac infarct (*A*) in the posterior wall of the left ventricle at the base just below the posterior cusp of the mitral valve (which is lifted up) Note the whitened thickened endocardium and the small patch of adherent pericardium (*B*) overlying the infarct. The left ventricular wall at the apex is somewhat thinner than usual but is not the site of any localized infarct. From man of 80 years of ge the acute coronary thrombosis had occurred at the age of 63

branches supplying each infarcted area, a fact of great significance in helping to explain various clinical, electrocardiographic, and pathologic anatomic discrepancies that have been noted in recent years. An interesting and important observation in this study was that, although in general there was agreement between the infarcted areas and disease of the particular arterial trunks directly supplying these areas, occasionally a recent thrombus was found in one coronary artery while the most recent infarct was located in an area supplied by the previously occluded opposite artery: obviously the area, before becoming infarcted, had been supplied by collateral anastomoses. Further evidence of the very complicated state of affairs in coronary thrombosis has been supplied by Sprague and Orgain (1935) in an analysis of 3,889 autopsied cases

at the Massachusetts General Hospital, 131 showed some degree of coronary occlusion but acute coronary thrombosis with occlusion limited to a single coronary artery or branch was found to be relatively infrequent, only 17 of 61 cases of acute coronary thrombosis showing such limitation, complete or recanalized thrombosis of a main artery or a main branch was discovered in the left coronary circulation in 46 cases and in the right in 21 In a recent analysis of a 20-year experience at the Massachusetts General Hospital the left coronary artery was found to be thrombosed much more commonly than the right and anterior wall infarcts were twice as common as the posterior and more serious as evidenced by the fact that of the 23 cases of rupture, 22 were through the anterior wall (Wang et al., 1948)

It has remained for Blumgart and Schlesinger (1940) to clarify much more fully this hitherto confused and difficult problem of the relationship between coronary occlusion, myocardial infarction and fibrosis, and clinical manifestations, by the study of 355 consecutive cases examined post mortem by special injection, roentgenologic, and dissection technic. They concluded (1) that in normal hearts intercoronary anastomoses, though present, are of little functional significance in obviating the untoward effects of sudden coronary narrowing or occlusion (2) that the apparent inconsistency between the presence of long standing obstructive arterial lesions and the absence of significant pathologic or clinical evidence of myocardial damage was dispelled by the demonstration of a collateral circulation (which had gradually developed) serving as a by pass in relation to the obstruction in each of these hearts (3) that in some instances of acute myocardial infarction caused by acute coronary occlusion the fresh thrombus may be found distant from the infarct in a vessel serving as a source for the collateral circulation supplying that area (for example, fresh infarction of the anterior wall of the left ventricle precipitated by a fresh occlusion in the right coronary artery which was serving as a source of collateral circulation to that area in the place of the old occluded anterior descending left coronary artery) and (4) that every patient suffering primarily from angina pectoris without evidence of valvular disease or arterial hypertension will show at postmortem examination old complete occlusion of at least one major coronary artery

Narrowing or occlusion of the smaller coronary branches may be completely compensated for by a rich collateral circulation often it is not so compensated, however and small localized areas of infarction result which are without symptoms or signs unless an especially important part of the heart is involved such as the atrioventricular node (of Tawara) and bundle (of His) with the production of heart block. Infarction of the base of the interventricular septum may lead to atrioventricular or intraventricular block or even to perforation of the septum.

Cardiac infarction results from the blocking off of blood supply to a part of the heart. There follows necrosis of the tissue (Figure 107) chiefly of the myocardium, often also of the pericardium if the infarct is large enough to extend to this structure, but infrequently of the endocardium which very probably receives

much of its blood supply directly from the ventricular chamber If the pericardium is affected a sterile fibrinous pericarditis occurs, and if the endocardium is involved a thrombus is likely to form over it in the ventricular (or rarely atrial) cavity Most intraventricular thrombi after cardiac infarction,



FIG. 107 Microphotographs of myocardial infarcts secondary to coronary disease. (*A*) Acute stage with invasion of leukocytes and beginning necrosis of muscle fibers. (*B*) Subacute stage with almost complete disappearance of damaged muscle fibers and beginning organization of scar with several small blood vessels. A few undamaged muscle cells remain near one of the small arteries. (C) Old fibrous scar involving part of the myocardium and penetrating to the endocardium (to the left) (Courtesy of Drs. F B and Kenneth Mallory Massachusetts General and Boston City Hospitals, Boston.)

however are laid down in the more or less stagnant pockets (sometimes frank aneurysms) where the infarcted heart wall is thinned and noncontractile even though the endocardium itself is intact. Such thrombi may form over old scars as well as over fresh infarcts (Mallory White, and Salcedo-Salgar 1939) It is from such intraventricular mural thrombi that emboli are frequently detached to cause serious complications after acute coronary occlusion, less often in the case of old scars it was largely to prevent such clots that anticoagulant therapy was introduced in the treatment of acute myocardial infarction. Infarction of the atria is rare, even if carefully looked for probably because the wall is thin and in large part supplied directly from the atrial cavities.

If the patient survives the immediate shock of the coronary occlusion and the acute cardiac dilatation and failure that sometimes follow the process of repair begins and is complete after some weeks or months (depending on the size of the infarct and the adequacy of the circulation in its neighborhood) leaving a fibrous scar of greater or lesser extent (Figure 107) In the process of repair there occur thinning and weakening of the ventricular wall which lead not rarely to cardiac aneurysm and during the acute stage even to rupture with fatal hemorrhage into the pericardium.

Rupture of the heart, when not traumatic or due to uncommon infectious processes (abscesses) is caused by recent, almost never by old, cardiac infarction from coronary occlusion such a mechanism is responsible almost invariably during the first ten to fourteen days of the infarct (Jetter and White, 1944 Friedman and White 1944) In a series of 270 cases of myocardial infarction among 2,967 autopsies at the Massachusetts General Hospital between March, 1933 and November 1940 cardiac rupture was found in 10 (3 7 per cent) all among the 105 cases of fresh infarction (9.5 per cent) and none among the cases with old infarcts, and the same percentage (9.5) was reported by Diaz Rivera and Miller in 1948 all in acute cases too this was in contrast to rupture of the heart in 16 (73 per cent) of 22 cases of acute myocardial infarction among psychotic patients in whom both diagnosis and treatment were difficult. Rupture involves the ventricular septum in some cases, actually 20 per cent of 76 among 28,657 autopsies reported by Furnam and Meneely (1948) it should be diagnosed correctly ante mortem although only five such were found among 36 collected in the literature by Rabinovich (1947) The papillary muscle may also rupture.

Sometimes lime salts or even bone are laid down in the old necrotic area of the infarct, as may also happen in a more gradual way in other parts of the heart from faulty circulation or disturbed metabolism, producing masses of calcification in papillary muscles or stony rings at the bases of mitral and aortic valves.

When there is marked narrowing of the coronary arteries, with or without actual occlusion here or there, angina pectoris and sudden death are quite common the myocardium itself may or may not show fibrosis or areas of infarction in such cases, but it is always ischemic. In their classic studies Blumgart

and Schlesinger (1937 1940) have presented evidence that temporary ischemia may cause irreversible myocardial changes, and that if the ischemia is of sufficient duration even without acute vascular occlusion myocardial infarction may result, of the same character and degree as that which occurs after permanent and complete coronary occlusion.

The heart may or may not be enlarged as the result of coronary disease with simple sclerosis and little or no strain on the damaged heart there is no change or possibly even a slight decrease in size, but with healing after a large infarction, especially if there is much strain, well-marked enlargement may result. Horine and Weiss (1935) who followed with roentgen ray study 20 patients who had a normal-sized heart at the time of coronary thrombosis found no evidence of enlargement over a period of nine months to nine years and ten months, but Bartels and Smith (1932) on the other hand in an autopsy study of the hearts of 42 cases of myocardial infarction in which all other known or supposed causes of cardiac hypertrophy (such as hypertension) were excluded, found definite gross cardiac hypertrophy in 37 (88 per cent) the average increase in weight above the estimated normal being 132 gm. My own experience is nearer that of Bartels and Smith, but it is the size of the infarct and the presence or absence of complications that determine whether or not the heart will be enlarged, when there is but a small infarct or angina pectoris alone without complications the size of the heart may remain within normal limits.

Cardiac aneurysms, ruptures of the heart, cardiac infarcts old and new and fatty and fibrotic changes of lesser extent have been known to pathologists for centuries, and their connection with coronary disease recognized post mortem for many years, but in the practice of medicine these conditions have been regarded as of much clinical significance and possible to diagnose readily only during the present generation.

Symptoms. The production of symptoms in heart disease of coronary origin is dependent on several factors in particular the sufficiency of the coronary circulation with relation to the degree of activity to which the myocardium is subjected, and also the speed of development of myocardial change, the extent of the damage, the adequacy of coronary arterial anastomoses, the amount of strain on the damaged heart, and the sensitiveness of the nervous system of the victim. If coronary narrowing and obstruction and even cardiac infarction develop slowly and there is no excessive cardiac strain, there may be no symptoms at all though there be extensive areas of damaged muscle and though one or both coronary arteries be occluded. The reserve strength of both myocardium and its blood supply is normally very great and not easily exhausted.

If however *sudden occlusion of a large coronary artery* occurs with inadequate collateral coronary circulation, the symptoms may be extreme, with terrible pain, shock, and sometimes death. Between these two extremes of symptoms in coronary heart disease from none at all to those that are overwhelming, there may be found all grades and varieties. Sometimes the symp-

toms, much exaggerated by nervousness or neurocirculatory asthenia in a particularly sensitive individual, are out of all proportion to the amount of heart damage and disability

The two most common symptoms of coronary heart disease are pain and dyspnea. It is difficult to obtain accurate figures for the relative frequency of these two symptoms since some old persons, though limited by slight substernal oppression or dyspnea on exertion, do not make much of these limitations which they ascribe to old age they may even find it difficult to distinguish between substernal oppression and dyspnea. On the whole, oppression is the more common symptom and is due to the inability of the damaged coronary arteries to maintain an adequate circulation in the heart muscle. Other symptoms also occur particularly palpitation, but they are less characteristic.

Pain in coronary heart disease is of different sorts and degrees. It may consist of slight, moderate or severe, high, mid, or low substernal oppression transient on exertion, that is, angina pectoris there may be extreme substernal and epigastric oppression, lasting for hours and sometimes followed by collapse, due to coronary thrombosis, or there may be slight to moderate precordial aching due commonly to an associated neurocirculatory asthenia. The precordial aching is more commonly found in other conditions than in coronary heart disease, the angina pectoris is infrequently found in other conditions, and the pain of coronary thrombosis is never like that found in other conditions except when it is atypical and so low in position that it simulates pain of gastrointestinal or gallbladder origin, or in very rare cases may be mistaken for the pain of a dissecting aortic aneurysm or for that due to pulmonary embolism The transient oppression due to coronary insufficiency that is, angina pectoris may almost exactly be simulated in position and character and duration by the discomfort due to spasm of esophagus or upper end of the stomach (cardiospasm) or indeed one symptom may excite the other· the differentiation is generally quite clear in the positive relationship of angina pectoris to effort.

The name "angina pectoris" (Latin *angina* from the Greek ἀγχόνη, strangling, and *pectus* breast bone or breast) was introduced by Heberden in 1768 to describe this characteristic symptom which has been also called "stenocardia.

Heberden, William. "Some Account of a Disorder of the Breast. *Medical Transactions* Royal College of Physicians, London, 1772, Volume 2, page 59 The original mention of angina pectoris was made by Heberden at a lecture before the Royal College of Physicians of London in July 1768, but not published until 1772.

The entire lecture is herewith presented, as published in 1772.

"There is a disorder of the breast, marked with strong and peculiar symptoms, considerable for the kind of danger belonging to it, and not extremely rare, of which I do not recollect any mention among medical authors. The seat of it, and sense of strangling and anxiety with which it is attended, may make it not improperly be called Angina pectoris.

"Those, who are afflicted with it, are seized, while they are walking, and more particularly when they walk soon after eating, with a painful and most disagreeable sensation in the breast, which seems as if it would take their lif away if it were to increase or to continue the moment they stand still, all this uneasiness vanishes. In all other respects the patients are at the beginning of this disorder perfectly well, and in particular have no shortness of breath, from which it is totally different.

After it has continued some months, it will not cease so instantaneously upon standing still, and it will come on, not only when the persons are walking, but when they are lying down, and oblige them to rise up out of their beds every night for many months together and in one or two very inveterate cases it has been brought on by the motion of a horse or a carriage, and even by swallowing, coughing, going to stool or speaking, or by any disturbance of mind. I have heard once and only one person, say that he had known it attack him, while he was up and standing still or sitting. But most, whom I have seen, have been perfectly unaffected with riding in any manner with speaking, swallowing, laughing, sneezing, or vomiting. One has told me, that this complaint was greatest in winter another that it was aggravated by warm weather in the rest the seasons were not suspected of making any difference.

"I have observed something like this affection of the breast in one woman who was paralytic, and have heard one or two young men complain of it in a slight degree but all the rest, whom I have seen, who are at least twenty were men, and almost all above 50 years old, and most of them with a short neck, and inclining to be fat.

"When a fit of this sort comes on by walking, its duration is very short, as it goes off almost immediately upon stopping. If it come on in the night, it will last an hour or two and I have met with one, in whom it once continued for several days, during all which time the patient seemed to be in imminent danger of death.

"When I first took notice of this distemper, and could find no satisfaction from books, I consulted an able physician of long experience, who told me that he had known several ill of it, and that all of them had died suddenly This observation I have reason to think is generally true of such patients; having known six of those, for whom I have been consulted, die in this manner and more perhaps may have experienced the same death, which I had no opportunity of knowing. But though the natural tendency of this illness be to kill the patients suddenly yet unless it have a power of preserving a person from all other ails, it will easily be believed, that some of those, who are afflicted with it, may die in a different manner since this disorder will last, as I have known it more than once, near twenty years, and most usually attacks only those who are above fifty years of ge. I have accordingly observed one, who sunk under a lingering illness of a different nature.

"The os sternl is usually pointed to as the seat of this malady but it seems sometimes as if it was under the lower part of it, and at other times under the middle or upper part, but always inclining more to the left side, and sometimes there is joined with it a pain about the middle of the left arm. What the particular mischief is, which is referred to these different parts of the sternum, it is not easy to guess, and I have had no opportunity of knowing with certainty It may be a strong cramp or an ulcer or possibly both.

"The opinion of its being a convulsion of the part affected will readily present itself to any one, who considers the sudden manner of its coming on and going off the long intervals of perfect ease the relief afforded by wine and spirituous

cordials, the influence, which passionate affections of the mind have over it; the ease, which comes from varying the posture of the head and shoulders, by straightening the vertebrae of the thorax, or by bending them a little backwards or forwards; the number of years, which it will continue without otherwise disordering the health; its generally bearing so well the motion of a horse or carriage, which circumstance often distinguishes spasmodic pains from those, which arise from ulcers, and lastly its coming on in certain patients at night just after the first sleep, at which time the incubus, convulsive asthmas, numbness, epileptics, hypochondriac languors, and other ills justly attributed to the disturbed functions of the nerves, are peculiarly apt either to return or to be aggravated.

"The pulse is, at least sometimes, not disturbed by this pain, and consequently the heart is not affected by it; which I have had an opportunity of knowing by feeling the pulse, during the paroxysms, but I have never had it in my power to see any one opened, who had died of it: the sudden death of the patients adding so much to the common difficulties of making such an enquiry, that most of those, with whose cases I had been acquainted, were buried before I had heard that they were dead.

But thought it be most probable, that a strong spasm be the true cause of this disorder, yet there is some reason for thinking, that it is sometimes accompanied with an ulcer, and may partly proceed from it: for I have seen two of these patients, who often used to spit up blood and purulent matter, one of whom constantly asserted, that he felt it come from the seat of the disorder. Another had a painful sensation in swallowing, and upon pressing the part, which seemed to be affected. From a fourth, who fell down dead without any notice, there immediately arose such an offensive smell, as made all, who happened to be present, judge that some foul abscess had just then broken.

Bleeding, vomits, and other evacuations, have not appeared to me to do any good. Wine and cordials taken at going to bed will prevent, or weaken, the night fits; but nothing does this so effectively as opiates. Ten, fifteen or twenty drops of Tinctura Thebaica taken at lying down will enable those to keep their beds till morning, who had been forced to rise, and sit up two or three hours every night, for many months. Such a quantity or a greater might safely be continued, as long as it is required: and this relief afforded by opium may be added to the arguments, *which prove these fits to be of a convulsive kind. Time and attention* will undoubtedly discover more helps against this teizing and dangerous ailment; but it is not to be expected, that much can have been done towards establishing the method of cure for a distemper hitherto so unnoticed, that it has not yet, as far as I know found a place or a name in the history of diseases.

Later Heberden added more cases of angina pectoris to his twenty-odd mentioned in the original lecture quoted above, and in 1786, in a chapter entitled "Pectoris Dolor" in his *Commentaries on the History and Cure of Diseases* (which was translated and published by his son, William Heberden, Jr. in 1802, a year after his own death) he wrote as follows: I have seen nearly a hundred people with this disorder, out of which number there have been three women.

Although coronary thrombosis is more likely than not to be attended by severe, exhausting, crushing substernal pain, often radiating to either arm or both arms, neck, head, or back as in angina pectoris, there are exceptions without any pain at all; in such cases there may be dyspnea instead or simply

collapse or prostration. In some groups of cases of coronary thrombosis the incidence of pain may be surprisingly low as in one series of 76 patients with coronary thrombosis proved at postmortem examination in which only 36 (47 per cent) gave a history of pain, 29 (38 per cent) gave a history of no pain, and the remaining 11 died suddenly (Davis, 1932) In another group of 100 cases reported by Gorham and Martin (1938) cardiac pain was noted in 58 per cent. In my own experience, however pain is more common than indicated by these figures a review of 56 consecutive unselected cases of my own, proved at autopsy has revealed the occurrence of pain in all but two (96 4 per cent) severe in 34 (61 per cent) moderate in 10 (18 per cent) and mild in 10 (18 per cent) (with the help of Dr E. W Miskall) The pain may be quickly masked by collapse or a moribund state or concealed by other symptoms or even by medication or alcoholism, or indeed on occasion not adequately sought for

The similarity of the character and the position of the pain of coronary occlusion to that of paroxysmal angina pectoris is a strong argument that coronary disease, by limiting the blood supply to the heart muscle, is the commonest cause of angina pectoris.

Dyspnea may vary from a slight breathlessness on exertion to the awful, struggling respiration of marked cardiac asthma dependent on the severity and suddenness of failure of the involved left ventricle which causes vascular engorgement of the lungs. Finally instead of pain as classically described, a sudden onset of dyspnea, with or without pulmonary edema, or of Cheyne Stokes respiration may also occur as an accompaniment of left ventricular weakness due to acute coronary occlusion or to chronic coronary heart disease, particularly in individuals with very limited myocardial reserve to start with. Moreover angina pectoris sometimes initiates such dyspneic attacks. Sighing respiration noted in occasional cases is due to the nervous state of the patient and not to his heart disease.

Palpitation is frequently complained of by patients with coronary heart disease, chiefly because of the occurrence of arrhythmia. Such arrhythmia is usually of relatively little importance, consisting as it does for the most part of premature contractions, chiefly of ventricular origin. However two additional observations should be made regarding premature beats and coronary heart disease In the presence of coronary insufficiency premature beats may on occasion be painful, due doubtless to the short diastolic rest, and, secondly premature beats induced by exercise suggest the possibility of an underlying deficiency of the coronary circulation. Occasionally paroxysmal auricular tachycardia and atrial fibrillation are also found as complications of coronary heart disease they are somewhat more important than premature beats. Finally paroxysmal ventricular tachycardia and atrioventricular block, either partial or complete, are the most serious disorders of mechanism which may occasion palpitation, the former is particularly of ill omen but fortunately very rare. These two disturbances of the heart beat will be discussed in Chapters 32 and 34 respectively

Prostration or collapse sometimes of high degree, is a frequent early symptom of acute coronary occlusion due to a state of vasomotor shock or peripheral vascular failure which may in itself be fatal In a few cases prostration, like dyspnea, may replace pain as the chief symptom of acute myocardial infarction especially in very old persons. Syncope as a much less important nervous reaction may be a rare complication, even in angina pectoris, and as such was once unnecessarily and confusingly designated syncope anginosa (Parry 1799)

Other symptoms occurring with coronary heart disease are either infrequent, unimportant, or due to complications. General weakness is occasionally seen in older persons who have arteriosclerosis elsewhere. The same is true of mental disturbances, faintness, dizziness, and even coma and convulsions, except that cerebral anemia due to high-grade heart block resulting from coronary disease may give rise to the *Adams-Stokes syndrome* (faintness, syncope, and convulsions, with a slow pulse) Prolonged coma lasting for hours or days, especially in aged persons, may follow rarely the temporary or prolonged drop in blood pressure that sometimes accompanies acute coronary thrombosis. Congestive failure may result in cough, hemoptysis, gastrointestinal symptoms, ascites, and edema. Sweating, restlessness, and vomiting are common symptoms at the onset of coronary thrombosis the vomiting, however is more often induced by the opiate used in treatment than by the heart attack per se. Hiccough is rare.

Coronary thrombosis leading to myocardial infarction usually causes *fever* for a few days with a temperature rising to 101 or 102 F rectally the grade and duration depending on the size of the infarct undergoing necrosis (Figure 108) Also the cardiac lesion may give rise acutely to various local pains due to visceral, cerebral, or peripheral embolism resulting from the discharge into the circulation of pieces of the mural thrombus in the left ventricle' pulmonary embolism may occur from thrombosis in the veins of legs or pelvis or from thrombi in the right ventricle, whether due to right ventricular (usually septal) infarction or to stasis.

Signs. There are frequently no signs of coronary heart disease, and the patient may give the appearance of perfect health. This is especially true in the case of uncomplicated angina pectoris on effort. When there is, however a high degree of coronary insufficiency there is often a rather characteristic sallow unhealthy tint to the skin suggesting on occasion slight jaundice or anemia. The patient is sometimes an obviously sick man at first glance, and this is particularly true during the state of shock that may occur at the time of an acute extensive coronary thrombosis.

A considerable amount of coronary disease may exist with little or no cardiac enlargement, but a very large myocardial infarct or congestive failure, whether limited to the left ventricle or involving the entire heart, is always attended by cardiac enlargement easily found both by physical examination and by roentgen ray The enlargement may come rapidly with cardiac infarction it then consists chiefly of dilatation of the left ventricle but it may involve

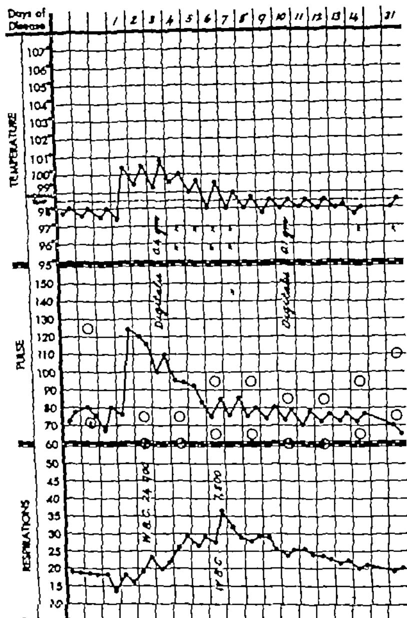


FIG. 108. Chart in acute coronary thrombosis causing large cardiac infarct, showing temperature (mouth), pulse rate, respiratory rate, and blood pressure. The patient, male, 5[illegible] years old, was in bed under observation and treatment for angina pectoris decubitus when the myocardial infarction occurred. He recovered but died suddenly a year later. Digitalization was carried out with beneficial results upon the onset of dyspnea due to dilatation and failure of the left ventricle. The blood pressure is designated by circles, open for systolic pressure and dotted for diastolic. The leukocytosis at onset was unusually high but quickly subsided.

also the right ventricle when the left ventricle fails as the process of repair goes on, hypertrophy develops, being apparently a compensatory measure. From coronary heart disease (thrombosis with infarction) alone the heart may increase in weight to 500 or 600 gm (normal weight about 300 gm)

The heart sounds are frequently weakened in coronary heart disease, especially the first sound at the apex shortly after coronary thrombosis sets in, sometimes a so-called tic-tac rhythm results from this weakening of the first sound. Gallop rhythm, protodiastolic in time, is especially common with left ventricular dilatation and weakness following coronary thrombosis. Reduplications and gallop rhythm may also occur with the development of intraventricular and atrioventricular block The pulmonary second sound becomes accentuated if the left ventricle fails. Murmurs may or may not occur the commonest is that of "functional" mitral regurgitation due to dilatation—an apical systolic murmur Basal murmurs are less common in coronary heart disease; an aortic systolic murmur may be found, due to aortic dilatation, resulting from an associated hypertension. Sometimes such a murmur is due to slight aortic stenosis caused by sclerotic involvement of the aortic valve, if aortic stenosis is marked, with systolic thrill felt over the aortic area, it is rarely to be ascribed to a simple atherosclerotic change in the aortic valve but more often to the result of an old infectious process with superimposed calcification. An aortic diastolic murmur is not found in coronary heart disease unless there is a complication of syphilitic aortitis, aortic stenosis with regurgitation, chronic hypertension with dilated aortic valve ring, or rarely senile ectasia of the aorta (see Chapter 28)

A pericardial friction rub frequently accompanies cardiac infarction, especially if the infarct is large It appears usually on the second or third day of illness and is transient, disappearing in a day or two—rarely it lasts for a week or more.

The arrhythmias found in coronary heart disease have already been mentioned (see page 541) the most common being premature beats and atrial fibrillation, the atrial fibrillation is either paroxysmal (about 33 per cent) or permanent (67 per cent) in type.

The pulse rate varies widely in coronary heart disease, from a normal range in most cases to a tachycardia of 120 or more in some cases with vasomotor shock or congestive failure in acute coronary thrombosis, or with abnormal rhythm rarely there is a bradycardia which may be marked (down to 30) if high-grade heart block supervenes.

The blood pressure in uncomplicated coronary heart disease is normal or low Severe cardiac infarction following coronary thrombosis is, however characteristically attended by a sharp fall in systolic blood pressure whether or not it has previously been high (because of hyperpiesia) The low blood pressure of 75 to 100 mm mercury systolic and 50 to 75 diastolic may continue for days, tending gradually to resume the level that existed before the coronary thrombosis or a somewhat lower level It is the combined result probably of vasodilatation, myocardial weakness, sedative drugs, and rest. In

a few cases the blood pressure is elevated by the pain during the acute episode of infarction I have encountered cases whose blood pressure was normal before and after the acute coronary occlusion but considerably increased at the time of the attack. In a good many other patients with small- and medium-sized infarcts the blood pressure is unaffected except for slight reduction with bed rest. During periods of higher degrees of coronary insufficiency (sometimes lasting for weeks) the diastolic pressure may be slightly elevated (to 95 100 or 105 mm)

Roentgenologic study may show no abnormality whatsoever though the aorta is often distinctly tortuous and elongated from atheroma, with prominence of the knob and sometimes with visible calcification. Roentgen ray examination usually shows cardiac enlargement after myocardial infarction and sometimes a bulge at or just above the apex due to a cardiac aneurysm (Figure 125 page 657) In the case of extreme cardiac infarction the action of the heart may be obviously weak, and the pulmonary artery and lung hilus shadows may be prominent due to pulmonary vascular engorgement secondary to failure of the left ventricle Fluoroscopy and kymography often reveal the site of the infarct as comprising a section of the left border of the heart shadow which shows little or no systolic pulsation or indeed even a paradoxical out thrust instead of retraction in systole In such cases as a rule, however the diagnosis is obvious by other methods of examination.

Calcified coronary arteries can sometimes be made out on the roentgenogram, but this finding is of little or no clinical value, since serious coronary heart disease may occur without it and since coronary calcification can be present without coronary insufficiency due to an adequate collateral circulation. Roentgen visualization of the coronary arteries is possible by retrograde aortic or arterial injection of contrast (Diodrast) fluid or by direct left ventricular puncture (see Chapter 7) but it would seem to be unwise to subject cases suspected of having coronary heart disease to a possible hazard in this procedure.

Electrocardiograms are of the greatest importance They are often normal with slighter degrees of coronary heart disease, especially between (not during) attacks of angina pectoris, but in advanced coronary heart disease they usually show changes in the Q and T waves and often in the S-T segments less frequently they show the presence of intraventricular block and low voltage uncommonly there is atrioventricular block. The commonest cause of heart block is coronary disease. Other disturbances of the heart beat are readily shown by electrocardiography Left ventricular preponderance is not commonly found unless there is an associated hypertension It may however follow myocardial infarction with left ventricular hypertrophy and dilatation.

There are a few relatively simple comments to make about the fundamental principles of electrocardiography in coronary heart disease before discussing detailed patterns. In the *first* place, there may be areas, small or large, of myocardium affected by the faulty blood supply sometimes the area is so microscopic that it may not show at all unless nodal or a-v conduction tissu

is involved, or such a large area or multiple areas are affected that the picture is very complicated one lesion neutralizing or confusing somewhat the effects of another It is surprising that so often the patterns are so clear-cut indicating isolated or preponderant lesions. In the *second* place, an effect on the electrocardiogram may be transient due to ischemia as during angina pectoris (Figure 109) or a combined effect of ischemia and of a destruction of muscle, old or new also In the *third* place, it is often possible to focus accurately over the

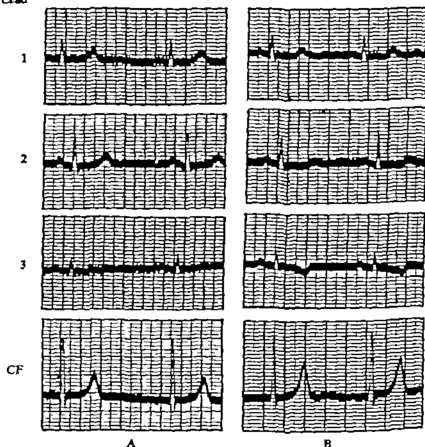


FIG. 109 Electrocardiograms taken during an attack of angina pectoris (*B*) and while free from pain (*A*) male, age 52. Note depressed *S-T* segments in Lead 2, sharp inversion of *T* waves in Lead 3 and unusually high *T* waves in Lead CF I the record during angina pectoris. Time = 0.04 and 0.20 second, amplitude 1 mm = 0.10 m

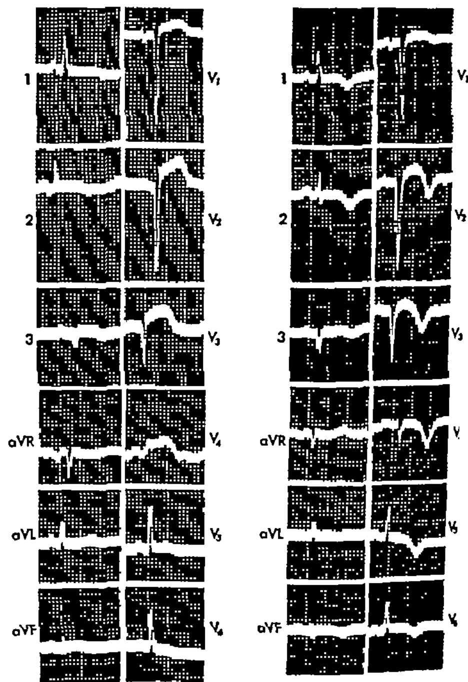
area involved by unipolar leads around the chest wall or in the esophagus or in the heart itself (by catheterization) which illustrates the value of multiple chest leads in fact even more, on occasion, than the six that have been routinely adopted. And here I would urge the use of the V leads of Wilson rather than those using one extremity as the indifferent lead point (see Chapter 9) In the *fourth* place it is important to remember that a myocardial lesion

is a dead or blind spot or "window" and so reflects the action current elsewhere, especially through the heart in the focus of the lead this accounts for the presence of a *Q* wave and the loss of an *R* wave (intrinsic deflection) over a myocardial scar In the *fifth* place, the left ventricle is where most of the effects of coronary obstruction are to be found, most commonly in the anterior wall, but quite often in the posterior wall and septum too and even in the lateral wall although that is more often involved with either an anterior or posterior wall lesion the right ventricle and the atria are per se uncommonly involved, quite possibly because of their thinner walls which are more readily supplied by the intracardiac blood stream or by a richer coronary network or both. *Finally* the electrocardiogram may change slowly or unexpectedly in coronary heart disease and therefore isolated records are often valueless serial records are not only desirable but often essential, even daily for weeks.

With these introductory remarks one may mention some of the coronary patterns, but for details and many illustrations the reader is perforce referred to textbooks on electrocardiography or on coronary heart disease per se. The earliest effect of coronary insufficiency on the electrocardiogram, whether due to temporary ischemia or muscle destruction, is an alteration of the baseline of the *S-T* segment (current of injury) (Smith, 1918 Pardee, 1920) This consists of an elevation of one or more millimeters (0.1 millivolt) immediately over the muscle affected and a depression over the opposite part of the heart.

Thus precordial Leads V and V_3 located over an anterior wall infarct will show an elevated *S-T* segment during its early stage (Figure 110 page 548) and an esophageal lead (over the posterior wall) a depressed *S-T* segment. In the case of a posterior wall infarct Lead V or V_8 will show a depressed *S-T* segment in the earliest stages (Figure 111 page 549)

Meanwhile the bipolar "classical" limb leads reflect these various changes reciprocally in Leads 1 and 3 (Figures 112 and 113) altered by a variable position of the heart, a fresh anterior wall infarct is likely to raise the *S-T* segment in Lead 1 and depress it in Lead 3 while a fresh posterior wall infarct may lower the *S-T* segment in Lead 1 and raise it in Lead 3 These characteristic patterns quickly evolve within a few days with a return of the *S-T* segments to the baseline and an inversion of the *T* waves in Leads V_4, V_5, and 1 in the case of an anterior infarct (Figure 110) and upright (normal) *T* waves in Leads V_4, V_5, and 1 but inversion (or increased inversion) of the *T* waves in Lead 3 (and often in Lead 2) (and in the esophageal lead) in the case of a posterior infarct (Figure 111) Finally with a large anterior myocardial infarct the *R* (intrinsic deflection) disappears and is replaced by a *Q* in Leads V_3, V_4, and V_5, a *Q* wave appears in Lead 1 along with persistence of inversion of the *T* wave for awhile or permanently (Figure 114) while with a large posterior myocardial infarct a *Q* appears or deepens in Lead 3 and at times in Lead 2 with persistence of inversion of the *T* waves in those leads for awhile and sometimes permanently (Figure 111 B) an esophageal lead in the case of a posterior infarct would show a *Q* wave and inverted *T* wave while the anterior precordial Leads V to V_6 inclusive tend to be normal. The



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FIG. 110. Electrocardiogram in anterior myocardial infarction, acute stage and later Female, ge 45 Not especially the bsence of *R* waves in Leads V to V inclusive b both *A* and *B* the elevated *S-T* segment in Leads 2, V V_4, and V of *A* and the lat inversion of *T* waves in Leads 1 2, and V to V inclusive of *B* Time = 0 04 and 0 20 second; amplitude 1 mm = 0.10 mv

Q wave appearance (which is not constant) and the T wave inversion gave rise originally to the expressions $Q\ T_1$ and Q_3T_3 types of infarction (Parkinson and Bedford, 1928) even before the exact sites of the infarction were identified. The T waves may or may not revert to normal in time but the Q waves remain as permanent evidence of the scars

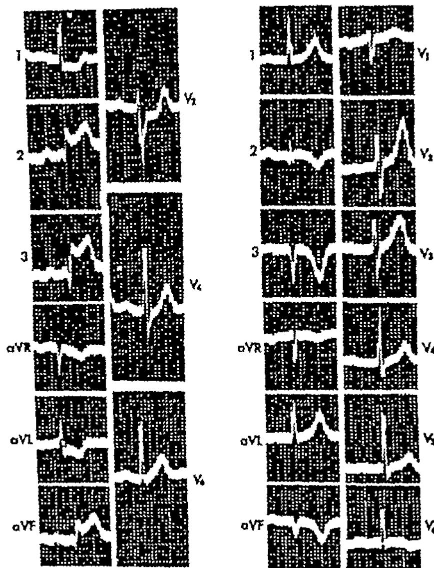


FIG 111 Electrocardiogram in acute posterior myocardial infarction, male, age 71 Note especially the greatly elevated S-T segments in Leads 2, 3 and aVF and the depressed S-T segments in Leads 1 and aVL in A and the Q waves and inverted T waves in Leads 2, 3 and VF in B Time = 0.04 and 0.20 second, amplitude 1 mm = 0.10 mv

The commonest patterns of myocardial ischemia and infarction have been presented, but there are two other sites which may occasionally be identified by electrocardiogram and still rarer ones (e.g., in atria or right ventricle) that require more exploration. A lateral wall infarct may show itself but little if it

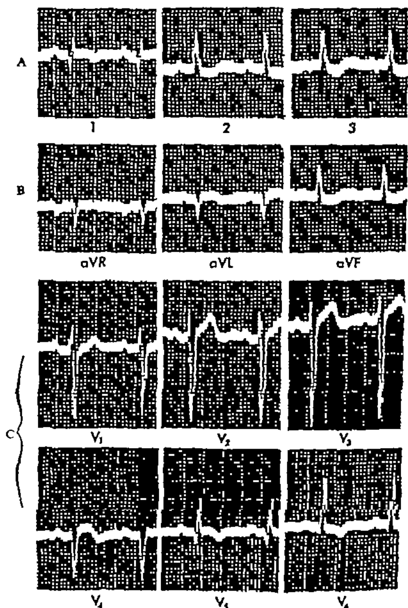


FIG. 112. Electrocardiogram in case of anterior myocardial infarction, showing reciprocal *S-T* changes in Leads 1 and 3 and *Q* waves and inverted *T* waves in Lead V. Male, age 54. (*A*) Bipolar limb leads 1, 2, and 3. (*B*) unipolar limb leads, VR, VL, and VF. (*C*) six precordial leads, V to V inclusive. Time = 0.04 and 0.20 second; amplitude 1 mm = 0.10 m

is small, Lead V_6 or V_7 may then reveal it by change in *S-T* segments and *T* waves. As a part of a larger infarct, anterior or posterior, it is easily identified (Figure 115) A septal infarct is also commonly associated with anterior or

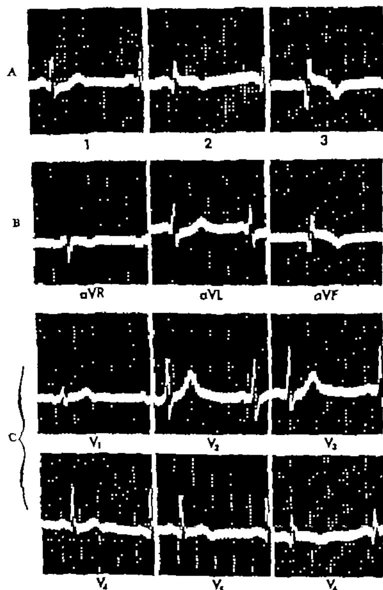


FIG. 113 Electrocardiogram in a case of posterior myocardial infarction occurring 48 hours previously and showing reciprocal *S-T* changes. Note also *Q* waves and inverted *T* waves in Leads 2, 3, VF and V Male, age 50. (*A*) Bipolar limb leads 1, 2, and 3 (*B*) unipolar limb leads, VR, VL, and VF (*C*) six precordial leads, V to V inclusive. Time = 0.04 and 0.20 second, amplitude 1 mm = 0.10 mv

posterior wall infarction but shows itself by changes in the precordial leads to the right of usual left ventricular lead points, that is, in V_2 and V_3 where changes in *S-T* segments, *T* waves, and *Q* and *R* deflections are found similar to those described for other infarct sites (Figure 116, page 554)

The unipolar limb lead records are less important as a rule than the precordial or bipolar limb curves in the case of coronary heart disease. They show

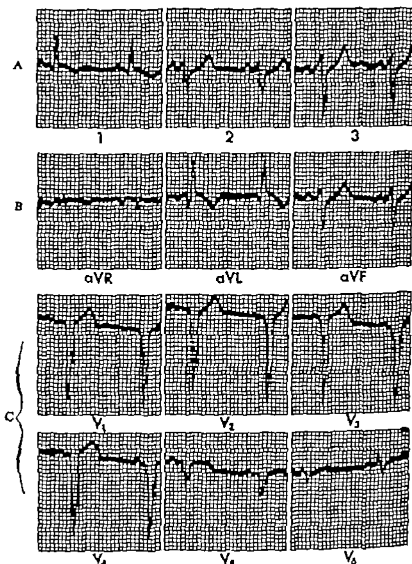


FIG. 114 Electrocardiogram in a case of chronic anterior myocardial infarct, male, age 65 (*A*) Bipolar limb leads 1 2, and 3 (*B*) unipolar limb leads, VR, aVL, and VF (*C*) six precordial leads, V to V inclusive. Note especially *Q* waves and inverted T waves in Leads 1 and aVL, and absence of *R* waves in Leads V to V inclusive. Time = 0.04 and 0.20 second, amplitude 1 mm = 0.10 m

patterns which vary with the heart position and so give information about both position and myocardial state. For example, an anterior infarct in the case of a horizontal heart will give upright *QRS* and *T* waves in Lead VR and inverted *QRS* and *T* waves in Lead VL while an anterior infarct in the case of a vertical heart will give upright *QRS* and *T* waves in Lead VF the limb (left arm or left leg) facing the *infarct* showing the most abnormality For other discussion of precordial leads the reader is referred to Chapter 9

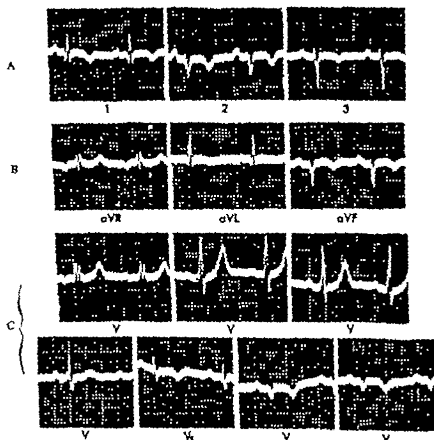


FIG 115. Electrocardiogram in a case of lateral infarct occurring one month previously male, age 57 (*A*) Bipolar limb leads 1 2, and 3 (*B*) unipolar limb leads, aVR, VL, and VF (*C*) seven precordial leads, V to V inclusive. Note especially Q waves in Leads 1 2, V and V absence of *R* waves in Leads 2, V and V nd inverted *T* waves in Leads 1 .. 3 aVL, VF and V to V inclusive. Time = 0.04 and 0.20 second; amplitude 1 mm = 0.10 mv

Other methods of examination reveal little of importance as a rule, though the grade and duration of leukocytosis resulting from sudden cardiac infarction is a useful clue to the size of the infarct and hence to the prognosis. Usually a polymorphonuclear leukocytosis of 12,000 to 15 000 is found for three or

four days, beginning a few hours after the onset of illness with an extensive infarct the white blood cell count may rise to 20 000 or more and remain elevated for a week or two. The sedimentation rate of the red blood cells is accelerated in acute myocardial infarction and remains rapid for weeks until the healing process is well established.

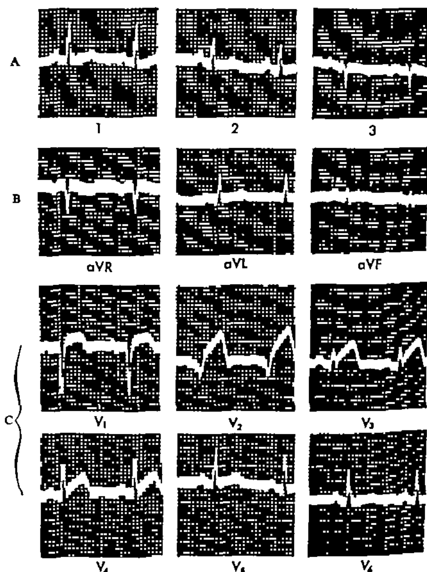


FIG. 116. Electrocardiogram in case of septal infarct, female, age 55 It is of interest that the limb leads show relatively little change while leads V and V are very abnormal with absence of *R* waves i V and elevated *S T* segments in V and V (*A*) Bipolar limb leads 1 2, and 3 (*B*) unipolar limb leads, VR, VL, and VF (*C*) six precordial leads, V to V inclusive. Time = 0.04 and 0.20 second amplitude 1 mm = 0.10 m

Course and prognosis. The course and prognosis of coronary heart disease are so variable that they must be considered individually in every case. The condition, unsuspected in life may be discovered only on postmortem examination after a noncardiac death in ripe old age or symptoms and signs may be marked and obvious in a fulminating acute catastrophe of severe coronary occlusion, cutting off the blood supply to a large mass of heart muscle, that may kill in a few hours or a few days. The prognosis depends not only on the degree and speed of involvement of the myocardium, but also on the treatment, the reserve strength of the heart, and complications.

When myocardial infarction sufficiently serious to be clinically recognized occurs, the prognosis must always be guarded, most cases, however survive the immediate attack, and half of the total survive for years, a good many even for ten years or more The first week is much the most hazardous, but danger of sudden death still exists during the second week even though all seems to be going well, after the first fortnight of acute myocardial infarction recovery is the rule. Of the series of 200 cases followed by Bland and White (1941) up to the time of death, or with survival for over 10 years, 38 (19 per cent) succumbed during the first month, while 50 (25 per cent) have lived more than 10 years, a much better record than was thought possible a decade ago The longest-lived proved case recorded to date survived nearly 40 years after his first attack of myocardial infarction at the age of 40 and kept at work till he was 77 (Drake, 1940) bettering the previous records of 17½ and 24½ years reported by myself in 1933 and 1937 records which had brought courage to many victims of this common condition. Just recently (1949) I reexamined a man whom I had seen at home 22 years earlier during a severe attack of acute myocardial infarction at the characteristic age of 52 years. Despite slight cardiac enlargement and an abnormal electrocardiogram he has been in excellent health for many years and plays 18 holes of golf without symptoms several times a week at 74 years of age he continues well in 1951 Undoubtedly long survivals are frequent though recognized only relatively recently

The prognosis is made worse in coronary thrombosis by the following findings advanced age a state of shock, an abrupt and prolonged marked fall in blood pressure, duration of severe substernal pain for more than twenty-four hours, fever for a week or more, especially when high at the onset (103 to 104 F) a high leukocytosis, especially if maintained for more than a week, rapid and marked cardiac dilatation, gallop rhythm ventricular paroxysmal tachycardia, heart block, pulsus alternans, pulmonary edema with or without cardiac asthma, dropsy and embolic phenomena. It has been noted that the symptom of angina pectoris tends to disappear when congestive failure or atrial fibrillation sets in or after coronary thrombosis, although angina pectoris may recur later It seems likely that this subsidence of angina pectoris is due in the case of congestive failure chiefly to restriction of activity of the patient, and in the case of myocardial infarction to the death of the muscle involved.

Paroxysmal coronary insufficiency as evidenced by the symptom of angina

pectoris on effort or even at rest (decubitus) has also, like myocardial infarction, a better prognosis than once was conceded. Many cases were in the past ruled out of consideration because they recovered, for it was not realized that there could be such an evolution. More careful analysis and longer follow-up of larger numbers of cases have doubled our expectation of the duration of life from an average of 4 to 5 years after the first symptom to one of 9 to 10 years (White, Bland, and Miskall, 1943) The explanation for such longevity and frequent recovery lies in the development of a more adequate collateral coronary circulation, a fortunate provision of nature. A recent follow-up report of 3 440 cases of angina pectoris listed 405 who had survived ten years or more (Montgomery et al., 1947)

Complications. In addition to such complications as myocardial infarction, cardiac aneurysm, cardiac rupture, congestive failure, heart block and other arrhythmias, and embolism from intracardiac mural thrombosis, coronary heart disease is frequently accompanied by hyperpiesia and general arteriosclerosis, sometimes by chronic rheumatic valvular disease, diabetes, nephritis, and cerebral hemorrhage or thrombosis, and less often by syphilitic aortitis, thyroid disease (either thyrotoxicosis or hypothyroidism) bacterial endocarditis, and congenital defects. It should be added that although general or peripheral arteriosclerosis and coronary disease are often associated, they frequently occur independently of each other One of the commonest of complications is indigestion, chiefly cardiospasm with gaseous distention of stomach or bowels, but sometimes gallbladder disease with or without stones; infrequently there is peptic ulcer The cardiospasm is largely reflex and not primary but the gallbladder disease is definitely more common in persons with considerable coronary disease than in those without, and vice versa (Walsh, Bland, Taquini, and White, 1941) this association is to be attributed not to a mutual causative effect but to some common factor dependent largely on the aging process in the type of persons affected. Finally even in the later years of life nervousness and neurocirculatory asthenia may occur to exaggerate the symptoms of coronary heart disease, and mental depression is frequently precipitated by the disability attending angina pectoris and particularly by the acute illness of myocardial infarction and the long but necessary convalescence, especially in the case of a strenuous middle-aged professional or business man never ill before.

Treatment. *Rest.* Of prime importance is limitation of activity to suit each individual case. For acute myocardial infarction such rest should be more or less complete for a few weeks more will be said about this below For angina pectoris decubitus the rest should be almost as complete until the condition ameliorates, since acute coronary thrombosis is almost invariably the cause even though myocardial infarction may not follow Even for angina pectoris on effort alone, it is often well at the onset to prescribe rest at home, though not in bed, until it is possible to appraise the situation adequately to determine the degree of chronicity of the disease, and to plan future action.

Drugs There is no specific treatment for coronary heart disease per se

unless it is due to syphilis, a rare cause, except for the quick relief of acute coronary insufficiency (angina pectoris) by the nitrites. The iodides, which have been used empirically for general arteriosclerosis, appear clinically to be inert, although experimental animals have been protected somewhat from atherosclerosis induced by high cholesterol diets when given potassium iodide. A definite increase of the coronary flow by vasodilatation has been reported experimentally from the use of theobromine and especially theophylline ethylene diamine (aminophylline) and occasionally favorable effects on angina pectoris and dyspnea have been noted clinically after the use of these drugs. Their trial is justified, but unless improvement is noted in the course of a week or two their continuance is not worthwhile; they are more likely to be effective when the coronary arteries are still able to dilate than in the case of rigid tubes. They may be administered by mouth in the dose of 10 gr 0.6 gm, of theobromine (or 15 gr 1 gm, of theobromine sodium salicylate, Diuretin) three times daily or preferably of 1½ to 3 gr 0.1 to 0.2 gm, of theophylline ethylene diamine (aminophylline) three to five times a day. The theophylline ethylene diamine (aminophylline) may be much more effectively given intravenously (0.24 gm in ampoule) or by suppository two or three times daily over short periods of time; the intramuscular injection is often painful.

Other drugs which have been recommended for the treatment of coronary atherosclerosis and for their effects on the heart have been in general disappointing, in fact often inert. Atropine was introduced hopefully to counteract a possible vagal factor in the production of coronary heart disease in man, having been shown to be effective in dogs, but its value has not been demonstrated. Choline and other lipotropic agents have been most recently used to delay, prevent, or even reverse somewhat the atheromatous process; they are effective in certain animals, especially the rabbit, but they have not yet passed in man beyond the experimental stage. Papaverine has been somewhat helpful in reducing the symptoms, in particular the pain, in coronary heart disease in the dosage of 0.03 to 0.09 gm (½ to 1½ gr) of the hydrochloride by subcutaneous injection twice daily or 0.09 to 0.20 gm (1½ to 3 gr) by mouth four times a day (Elek and Katz, 1942) but it is often disappointing. Testosterone has little or no value unless there is a specific endocrine need thereof. The same is true of vitamin E and other vitamins. Tissue extracts in general have been of little value. Cactus is inert. Cobra venom has been recommended for intractable pain but has not become established.

One of the newly introduced drugs for the prophylaxis of angina pectoris, apparently by the production of vasodilatation, is khellin, an active principle from the seeds of visnaga, a plant growing in the Eastern Mediterranean area given in the dosage of 100 mg intramuscularly daily or 50 mg by mouth one to three times a day (Anrep, et al., 1947 1949 Armbrust and Levine, 1950). In larger dosage this drug may cause nausea although its therapeutic effect has seemed favorable it is often toxic and needs further appraisal before widespread routine adoption.

Perhaps the most useful drugs to date for obstinate severe angina pectoris,

both introduced to depress thyroid function, have been thiouracil or better methylthiouracil (0 2 to 0.6 gm daily) and irradiated iodine to accomplish a medical thyroidectomy (Blumgart, Freedberg, et al. 1948 1950) The latter procedure offers the greater promise with less hazard of the first 18 cases tried (of coronary or myocardial insufficiency more commonly the former) 6 have proved to be highly successful and 6 others improved, while 6 were failures the dosage has averaged about 50 millicuries divided into 2 or 3 weekly administrations in water by mouth, an average of 5 to 6 weeks elapsing before noticeable relief accompanying a drop of basal metabolic rate, which is kept from descending too far by small amounts of thyroid.

Of prime import is the fact that in many cases there slowly but spontaneously develops an adequate collateral coronary circulation and while that is going on nitrites in particular nitroglycerine (0.3 to 0 6 mg or 1/200 to 1/100 gr) and erythrol tetranitrate (15 to 30 mg or ¼ to ½ gr) may be used, often very effectively prophylactically as needed or regularly to tide over many weeks or months of trouble during which care should be exercised to avoid undue strain physical or emotional. I have found this procedure often the best of all.

For the immediate therapy of angina pectoris the nitrites are most useful, for congestive failure as evidenced by dyspnoea or edema (pulmonary or systemic) digitalis and diuretics (see Chapter 30) for coronary thrombosis with myocardial infarction and cardiac asthma morphine and, if there is not adequate relief thereby a trial of oxygen by inhalation, or of aminophyllin by vein for ventricular paroxysmal tachycardia quinidine and for atrial fibrillation digitalis or quinidine In the case of coronary thrombosis it may be necessary to give large amounts of morphine, even intravenously to control the pain, often as much as ½ to 1 gr in divided doses in the course of a few hours, or caffeine for collapse It is wise, however to give no more morphine or its derivatives than is absolutely necessary because of the nausea the strain of vomiting, constipation, and the depression that commonly result. If morphine does not in some cases control the very prolonged pain of myocardial infarction it is reasonable to try the effect of oxygen inhalation or of aminophyllin intravenously or of papaverine (0.2 gm, 3 gr by mouth or 0.1 gm, 1½ gr intramuscularly) these measures are usually disappointing but sometimes they help A ration of 0.2 gm (3 gr) of quinidine sulfate every 4 to 6 hours during the first 2 weeks of acute myocardial infarction or in cases of angina pectoris decubitus may prevent ventricular tachycardia and fibrillation it should be used routinely as a measure to reduce mortality in coronary heart disease (Borg, 1939)

All of the various nitrites act by their vasodilating effect, either directly to improve the coronary circulation by increasing its volume, or indirectly by decreasing peripheral arterial resistance to relieve the work of the heart, or more probably by both of these actions. The most potent and rapid in effect of all the nitrites is the volatile *amyl nitrite* introduced by Brunton in 1867 It is inhaled from a small glass container (pearl or ampoule) broken at the

moment it is needed, usually the amount in each container is 2 or 3 minims (0 12 to 0 18 cc) Inhalation causes in a few seconds flushing of the face, pounding of the pulse in the head and all over the body and relief of the angina pectoris If inhalation is long continued, dizziness and a disagreeable headache may result. *Nitroglycerine* (glyceryl trinitrate, glonoin, or trinitrin) introduced by Murrell in 1879 is, after amyl nitrite, the next most rapidly potent nitrite, being absorbed in a minute or two, with relief of angina pectoris and with the production of symptoms and signs of vasodilatation It is best taken in the form of a quickly soluble tablet containing 1/200 gr (0 0003 gm) of nitroglycerine crushed and held in the mouth for rapid absorption It must be reasonably soft, fresh, and potent, for sometimes the tablets are hard or become old and relatively inert. If the dose of 1/200 gr is ineffective 1/100 gr may be used, but it is better to try first the smaller dose in any given case since it is often sufficient and does not produce so many disagreeable reactions—flushing, headache, pounding pulse, faintness, and even syncope—to which some persons are subject, even smaller doses, 1/400 gr (0 00015 gm) or less, are sometimes adequate especially for prophylactic use (see below)

Nitroglycerine is in most respects preferable to amyl nitrite in the treatment of an attack of angina pectoris, for it is easier to carry and to use (not requiring the breaking of a glass container) is effective enough without being disagreeably and unnecessarily potent, and its lower cost favors its constant use when needed rather than its reservation for rare occasions. Less important is *sodium nitrite* introduced by Hay in 1883 which, in the dose of ½ to 1 gr (0 03 to 0 06 gm) in tablet form by mouth, is rather slow in its effect, requiring five to ten minutes, but has the advantage of a longer continued effect (an hour or more) hence it can be used somewhat in a prophylactic way For immediate therapy it is far inferior to nitroglycerine and amyl nitrite its actual effect is, however similar Next comes *erythrol tetranitrate* introduced by Bradbury in 1895 taken in ¼ to ½ gr (0 015 to 0 03 gm) doses in tablet form by mouth, it is more valuable than sodium nitrite because its effect lasts for several hours, it is very slow in its action, taking fifteen to thirty minutes to produce the usual nitrite effect. *Mannitol hexanitrate* introduced by Bradbury in 1895 and *mannitol pentanitrate* introduced by Marshall and Wigner in 1902, rarely used in the past, have been recently revived, they are taken in 1 gr (0 06 gm) doses in tablet form, are very slow in their action, requiring one hour to produce full effect, but they continue to be effective for five or six hours. Finally *octyl nitrite a liquid less volatile and effective than amyl nitrite, has recently* been introduced, rather to be used prophylactically than in the direct treatment of an attack of angina pectoris administered by inhalation, it requires 30 seconds for its effect which lasts about 20 minutes, it has not established itself as at all preferable to the nitrites already in use. The last nitrites mentioned are primarily for prophylactic use, erythrol tetranitrate being preferable although expensive and likely to give rise, as are also the other preparations, to obstinate and disagreeable headaches. The following table summarizes the speed and duration of action of the various nitrites.

Table 10

THE SPEED AND DURATION OF ACTION OF VARIOUS NITRITE DRUGS

Preparation	*Speed of action*	*Duration of effect*
Amyl nitrite	A few seconds (10)	A few minutes (10)
Octyl nitrite	30 seconds	20 minutes
Nitroglycerine	1 to 2 minutes	30 minutes
Sodium nitrite	5 to 10 minutes	1 to 2 hours
Erythrol tetranitrate	15 minutes	3 to 4 hours
Mannitol hexanitrate or pentanitrate	30 minutes	4 to 5 hours

The most effective drug after the nitrites is *alcohol*, it was used routinely one hundred years ago before the introduction of the nitrites, and even now when the nitrites are not available an ounce or two of whisky brandy or rum may give quite rapid relief from angina pectoris, usually in the course of a very few minutes. However inasmuch as a paroxysm of angina pectoris is likely to subside before alcohol exerts its full effect, these various beverages are more useful in prevention than in treatment, and inasmuch as alcoholism as a habit may be established by this procedure, the prophylactic use of nitroglycerine is much to be preferred. It should be added that although heavy drinkers seem to show little atheroma, the moderate or even the considerable use of alcohol does not protect against coronary heart disease in middle age, I have encountered a good many patients who have proved this point.

Other drugs for the immediate treatment of angina pectoris are either less effective than the nitrites and alcohol or inadvisable. Ether and chloroform were sometimes used in treatment in place of alcohol in the early days before the introduction of the nitrites, but now there is little place for them they may be effective in severe prolonged attacks. Bromides are of little use except to calm nervous excitement. Morphine is too slow in its action and is far less effective than the nitrites It should be avoided in the vast majority of cases and simply reserved for severe long-continued pain, not relieved by an effective nitrite and generally due to myocardial infarction. Serious drug addiction and psychoneuroses have frequently followed the unwise use of opiates in the treatment of angina pectoris. Digitalis and strophanthin do not relieve angina pectoris, in fact they may aggravate it, but they can be used without fear to relieve congestive heart failure or to control the ventricular rate of atrial fibrillation in spite of the presence of attacks of angina pectoris.

Diet. Much has been said and written about the relationship of diet to coronary atherosclerosis (the basis of 99 per cent of coronary heart disease) but most of it is still conjecture and opinion. It is certainly true that the deposition of cholesterol in the coronary arterial intima is the fault with which we are concerned, that cholesterol foods are richly ingested in this country and that "coronary patients" and "candidates" are prone to have high cholesterol contents in their blood. But, as stated earlier in this chapter under Etiology doubtless much, if not the major part of this blood cholesterol is

of endogenous origin, associated with metabolic processes, and not exogenous. The total calories of a rich diet may well be most important of all.

In the present state of our knowledge it would seem wise to maintain a diet of moderation, *low in cholesterol foods* (especially eggs, butter cream, and cheese) in robust persons with coronary heart disease or who look like candidates. It probably is not necessary or wise to exclude these fats completely but it does appear advisable to treat obesity to recommend limited caloric intake (according to activity) to avoid large or rich meals, and perhaps to limit also heavy use of tobacco Alcoholic beverages may be permitted provided their caloric values are taken into consideration, but they do not have any special virtues.

Control of various activities, care of bowels, and sometimes hospital or sanitarium treatment are necessary in the therapy of coronary heart disease and its complications. Much attention may be needed in a chronic case to prevent the occurrence or recurrence of serious complications, but each patient must be considered individually on each occasion and not be made to follow any set rules. It need only be said that any activity or strain of doubtful effect should be avoided, unless the patient is thereby too depressed or unhappy A balance must always be sought between too much and too little restriction of life, not only from the standpoint of longevity but also from that of happiness.

Acute coronary thrombosis must be regarded more seriously than most cardiac conditions, abd careful rest for weeks or months (a minimum of three to four weeks) should be prescribed in order to assure as sound a healing of the myocardial infarct as possible, with a very gradual and careful convalescence (a minimum of one month after completing the rest period) by wise treatment at the start, life may doubtless be prolonged for many years in some cases. At times shortly after coronary thrombosis when the patient is feeling well and therefore possibly too active, sudden death from cardiac rupture or other cause may occur sometimes, however this accident is not preventable. *Sutton and Davis (1931) made the interesting observation that in dogs* rest for six days after the production of cardiac infarction permitted the formation of a small well-contracted scar without thinning of the wall of the ventricle, while exercise within three days of the infarction produced aneurysmal bulging of the ventricular wall with a thin scar The absolute need of complete rest for two weeks after a large acute myocardial infarction in man has been clearly demonstrated by the finding of rupture of the heart during the first twelve days in 16, or 73 per cent, of 22 psychopathic patients, in contrast to only 10 cases, or 9.5 per cent, of 105 patients in the wards of a general hospital (Jetter and White, 1944 Friedman and White, 1944)

As the result of experience during the last twenty-five years I have found that a very satisfactory plan of treatment for the average case of acute myocardial infarction is one month of full rest (the first fortnight very quiet to avoid so far as possible serious complications, in particular *dilatation and* rupture of the heart during the critical period of softening of the wall and the beginning of the laying down of the scar) one month of gradually increasing

activity (the first week in a chair a little more each day the second week walking on the level increasing distances, the third week going slowly over the stairs once a day and the fourth week going out for short daily rides, weather permitting) and a third month if possible (although this is not always essential) to consolidate the recovery nervously as well as otherwise. One may need to lengthen or shorten these three periods of the convalescence as circumstances demand. It is of importance to realize that the heart may recover more rapidly than the depressed mental state which is so often a complication. Too long a stay in bed or too long a total convalescence is bad for the morale and the general health. During the last two decades the pendulum has swung from one extreme to the other with respect to the length of time at full rest and of total convalescence from two or three months of the former and six months to a year of the latter to a few days only at rest and a few weeks only away from work. The wisest course is doubtless to avoid both these extremes.

An important consideration in the treatment of acute myocardial infarction, which has been much debated is that of bed rest versus rest in a chair. In mild cases with small infarcts there is no reason why the patient may not sit in a comfortable chair by the bedside even during the first week, avoiding, however physical exertion. Also if a patient is very ill and has orthopnea or otherwise is uncomfortable recumbent he may be lifted into a suitable large chair or better still use a chair-bed (see Chapter 30) In any case a bedside commode for bowel movements is for many persons better than a bedpan since its use is much less of a strain. Bathroom privileges are best reserved until after the first fortnight. And finally quiet exercise of the legs daily while still otherwise at full rest is advisable to help prevent leg vein thrombosis.

A limited diet to maintain a low basal metabolic rate during the process of healing of the infarct has been advised also (Master et al. 1935) but this in extreme degree is usually unnecessary and probably at times unwise. A light mixed diet of 1 800 to 2,100 calories in 4 or 5 small meals a day is a good plan. In the case of an obese patient a low calorie diet is in order and if congestion threatens the diet should be low in sodium.

Other measures In recent years several new measures of treatment have been introduced to control certain manifestations or complications of coronary heart disease. Paravertebral alcohol injections of the sympathetic nerve connections to the heart have been largely supplanted by sympathectomy itself but this procedure too is now rarely indicated, in part because of the reversibility of the coronary heart disease in time in the majority of cases even of severe angina pectoris (including the decubitus type) by patience and medical therapy in particular free use of the nitrites often tiding over the disagreeable and hazardous period of serious illness, and in part because of the superiority of irradiated iodine therapy (mentioned above) in the most obstinate cases. The principle of total thyroidectomy ingeniously introduced in 1933 and soon abandoned has been recently revived as the medical measure just referred to. Much direct surgery on the heart has been attempted to bring new blood supply by constructing anastomoses to the coronary circulation. Beck has

been a leader in this field (1935 and since) and although many of the results have been disappointing, especially in establishing pericardial adhesions (also produced via the omentum by O'Shaughnessy 1937 and via powdered substances) new trials are in progress consisting most recently of grafting a systemic (e.g. brachial) vein into the coronary sinus and, later on, partially occluding the sinus. Fauteux (1941 1946 and 1948) performed much original work on the heart to improve the coronary circulation by ligating the great cardiac vein and to reduce the hazard of ventricular fibrillation by coronary neurectomy but these procedures, though promising, are still hazardous in man.

Anticoagulants, both heparin and dicoumarin, but especially the latter have been, in the last decade, introduced in coronary heart disease for two purposes. Complications of thrombosis and embolism, both pulmonary (chiefly from leg vein clots) and systemic from intracardiac thrombi, mostly over a healing infarct, have been distinctly diminished by anticoagulant therapy begun at the earliest stage of acute coronary thrombosis with myocardial infarction. With or without initial heparin (which may prove wise if readily available) Dicumarol is given the first day usually in the dosage of 200 mg after a test of the prothrombin time has shown no abnormal delay and provided daily tests of the prothrombin time of the patient's serum can be accurately determined. A daily dosage of 50 to 100 mg or none at all is given thereafter during the next three or four weeks to maintain a prothrombin concentration of 20 to 50 per cent of the normal. Wright not long ago (1948) analyzed 800 cases of acute myocardial infarction, half of whom received Dicumarol and half observed as controls the mortality was 13 per cent in the treated patients and 23 per cent in the controls, and there were thrombo-embolic complications in only 13 1 per cent of the treated cases in contrast to 41 8 per cent of the controls. A new oral anticoagulant more rapidly acting than Dicumarol, called Tromexan, is now on trial (Wright, 1951)

Less amenable to proof, the other purpose for anticoagulant therapy in coronary heart disease has been to prevent or delay coronary thrombosis itself. This is still in the experimental stage and may prove to be both impractical and ineffective. It may have to be continued for years and during its use the blood must be tested frequently (daily or every few days) to be safe, for the hazard of hemorrhage exists as well as of ineffective dosage. To combat serious effects of anticoagulants, certain measures have been introduced the most effective is vitamin K oxide (0.5 gm or more intravenously) whole blood transfusions have yielded minor temporary benefit (James, et al. 1948) As a matter of fact, vitamin K has even been recommended in the treatment of coronary disease in certain cases with the idea of preventing hemorrhage in the coronary wall (Doles, 1947) but confirmation of this is still lacking.

Last, but not least, one must treat the state of shock which not rarely complicates acute coronary thrombosis or acute myocardial infarction. Simple measures of absolute rest and quiet and nursing care with strong coffee by mouth and aminophyllin intravenously may suffice in mild cases, but in serious shock,

something radical may be needed to save a life. Here transfusion with care under close observation may be helpful—up to 250 or 300 or more cc slowly given, watching carefully for overloading of the veins, pulmonary and systemic, in the face of a weak heart muscle. Plasma may be given instead of whole blood.

Finally in all the therapy of coronary heart disease one must not lose sight of the very important facts (1) that the heart itself possesses a striking recuperative capacity no matter what is done, but (2) that great care in all details of physical activity and nervous strain, in exposure to weather and in eating and other habits may be essential for survival over periods of acute or subacute trouble.

Differential diagnosis. Chronic coronary heart disease is often very difficult to discover and in the stage of congestive failure with arrhythmia may be hard to distinguish from rheumatic heart disease or thyrotoxic effects. The age of the patient, a history of angina pectoris, the usual absence of characteristic murmurs of chronic valvular disease, the usual absence of much cardiac enlargement, the finding of tortuosity of the aorta by roentgen ray and of intraventricular block, or other even more specific "coronary" electrocardiographic patterns help to establish the correct diagnosis. Myxedema, too, has been occasionally confused with coronary heart disease on the basis of the electrocardiograms which with abnormal *T* waves and low voltage of the *QRS* waves may be indistinguishable in the two chronic diseases; however the appearance and symptoms of the patient readily reveal the myxedema, confirmed by the very low basal metabolic rate. These diseases may coexist.

Acute coronary occlusion with cardiac infarction has been frequently confused in the past with *acute abdominal disease* such as acute indigestion, gallstones, and perforated peptic ulcer and laparotomy has been done in some cases by mistake. Although position of the pain, fever leukocytosis, and gastrointestinal symptoms like vomiting may be common to the two conditions, there are usually enough differences to make the distinction fairly certain. The most important point in this differentiation is the past history in the one case a story of angina pectoris or other cardiac symptoms or signs, and in the other a record of indigestion or colic. Other signs and symptoms of importance in differentiating coronary thrombosis and acute abdominal disease are first to be found in the cardiac examination which may show characteristic abnormalities, namely dilatation, poor sounds, pericardial friction rub, and specific electrocardiographic findings such as *T* wave changes and intraventricular or atrioventricular block. Secondly the abdominal examination may show masses, definitely localized tenderness, or spasm, or there may be jaundice or bleeding from the gastrointestinal tract. Thirdly the pain in myocardial infarction is more often high under the sternum or both substernal and epigastric, rarely epigastric alone, and is very frequently referred to the arms, especially the left. And fourthly the victims of coronary thrombosis are preponderantly elderly or middle-aged men, while acute abdominal disease is common in middle-aged women as well as in men. Despite the greatest care, however if

a diseased gallbladder is unusually high in position, acting almost like an intrathoracic organ, it may be mistaken for an infarcted heart in the presence of some coincident coronary heart disease.

There are four other conditions that are especially likely to be confused with acute coronary occlusion, they are acute pericarditis, dissecting aortic aneurysm, pulmonary embolism, and mediastinal emphysema. The first, *pericarditis* is commonly misinterpreted, particularly in young adults in whom the error can be serious both from the standpoint of prognosis and from that of treatment and of the plan of life: the differentiation is as a rule easy in two particulars precordial pain that is felt preponderantly or only on respiration and little if at all when the breath is held is due as a rule to acute pleuropericarditis and not to myocardial infarction, and an electrocardiogram that shows very little or very transient or unusual abnormalities (such as transient elevation of the *S-T* segments or flattening or inversion of the *T* waves in all leads) points much more to pericarditis than to myocardial infarction. The youth of the patient is often a clue, but the severe long-continued pain, fever leukocytosis, and pericardial friction rub may easily lead one astray *Dissection of the aortic wall* is to be distinguished by the very abrupt onset of most severe pain (not working up to a crescendo as in most cases of coronary thrombosis) the reference of the pain almost invariably to the back and often down to the legs, the evidence of obstructed circulation in the branches of the aorta, especially the iliac and femoral arteries, the relatively normal electrocardiogram, and the almost constant presence of chronic hypertension. In the case of *pulmonary embolism* there is usually a story of recent surgical operation or injury association with thrombophlebitis, more often severe dyspnea or prostration than severe pain, and normal or characteristic electrocardiogram (if the acute cor pulmonale is present) (see Chapter 20) the chief difficulty with respect to this particular differential diagnosis is that both conditions not rarely occur together in the same patient, one leading to the other *Mediastinal emphysema* (Hamman, 1937) is fortunately very rare but it may be very confusing and give rise temporarily (that is, for a few hours) to symptoms and signs that simulate acute myocardial infarction there may be intense substernal pain and a state bordering on shock, the heart sounds may be weakened or attended by crepitations which might casually be confused with friction, there may be a temporary change in the electrocardiogram and slight fever and leukocytosis, but the differentiation should not be difficult if this condition is borne in mind because of the rapid clearing of the signs and symptoms and the usual finding of air in the mediastinum or even under the skin.

Besides these five conditions with which acute coronary occlusion may readily be confused there are many other diseases which may more or less uncommonly be mistaken for it. Herrick (1935) listed 28 different conditions which he had himself seen mistaken for coronary thrombosis, they are as follows paroxysmal angina pectoris, cardiac arrhythmia, cardiac neurosis, neurocirculatory asthenia, malingering, acute pericarditis, syphilitic aortitis with and without aneurysm, dissecting aortic aneurysm, pleurisy pneumonia,

carcinoma of bronchus and lung, massive collapse of the lung, pneumothorax, pulmonary embolism herpes zoster arthritis of costochondral articulation, shoulders, and spine, bursitis, gallstones, peptic ulcer carcinoma of stomach or duodenum, acute gastritis, spastic colitis, diaphragmatic hernia, tabetic crisis, and impending diabetic coma. Diaphragmatic flutter might be added to this list.

Finally angina pectoris as a symptom of coronary heart disease may likewise be overdiagnosed, most commonly when there is indigestion with cardiospasm (with or without a hiatus or diaphragmatic hernia) neurocirculatory asthenia, or cardiac arrhythmia. Angina pectoris as a characteristic symptom of coronary insufficiency due primarily to coronary atherosclerosis has been well described earlier in this chapter especially in the quotation from Heberden. It is closely simulated only by spasm of esophagus or cardia of stomach (cardiospasm) from which it is to be, as a rule, readily distinguished by its relationship to effort rather than eating and by its more rapid response to nitroglycerine.

If in rare cases who are not gravely ill, there is serious doubt about the diagnosis of coronary insufficiency recourse may be made to exercise tests such as customary walking or stair-climbing or Master s two-step test, or to Levy s anoxemia test.

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SEE ALSO REFERENCES UNDER CHAPTER 9 ELECTROCARDIOGRAPHY AND 25 MYOCARDIAL DISEASE

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CHAPTER 22

NEUROCIRCULATORY ASTHENIA (DA COSTA'S SYNDROME, ALSO CALLED THE SOLDIER'S HEART "EFFORT SYNDROME," AND ANXIETY NEUROSIS) CARDIAC NEUROSIS AND PSYCHOSIS

NEUROCIRCULATORY ASTHENIA

Introduction. Despite considerable research on this mysterious malady since the last edition of this book and the elucidation of certain of its aspects, the fundamental mechanism still eludes us and we have as yet no specific therapy. The chapter therefore requires relatively slight changes.

Neurocirculatory asthenia also called less adequately "the *soldier's* heart," "effort syndrome," and "the anxiety neurosis" is an important condition of instability and abnormal irritability of the nervous and circulatory systems, of unknown cause. It tends to be precipitated as an acute disorder in many persons by physical exhaustion, nervous strain, and infections, and so constitutes a kind of fatigue syndrome, in some individuals, however who appear to be "constitutionally inadequate," it is a more or less chronic condition, usually associated with, or a part of, a psychoneurosis of the anxiety type. It is not in itself disease of either heart or nervous system but a functional circulatory and nervous disorder often confused or associated with heart disease; hence it forms an essential part of this book.

In the present state of our knowledge, and until the problem is solved, I would suggest the following definition *Neurocirculatory asthenia is a condition of ill health characterized by a group of symptoms consisting of dyspnea (often with sighing respiration) palpitation, exhaustion precordial pain (most often an ache) dizziness nervousness and sometimes tremor sweating headache and syncope aggravated by effort or excitement and attending or following anxiety neuroses infections or physical or nervous strains especially in hypersensitive individuals who in extreme cases may show the condition more or less constantly with little or no provocation.* That such a

state of ill health exists there can be no doubt, no matter what its pathogenesis or exciting factors. Until we can give it a fundamentally better designation, the descriptive term neurocirculatory asthenia seems still to be the best. It is neither fatigue per se, nor infection, nor thyrotoxicosis, nor nervous strain, nor psychoneurosis it is a state of ill health which may attend or follow any of these conditions or indeed others too, or even frequently stand alone.

Physical effort of extreme degree will always produce symptoms of circulatory distress, but fatigue of skeletal muscles or of nervous system may prevent such effort. The symptoms of circulatory distress are dyspnea, palpitation, and precordial or substernal oppression, alone or combined. Generally associated with them are weakness, and often dizziness, faintness, and tremor The combination of these symptoms occasioned by exertion has been called the effort syndrome. Such effort syndrome may be induced easily in weak, tired, sick, or nervous persons, and with difficulty in strong, well-trained, and calm individuals, whether heart disease is present or not. Even a perfectly normal person, if sufficiently strenuous, will show the syndrome in some form, perhaps having dyspnea alone, palpitation, substernal or precordial oppression, or two or three of these symptoms together It is likely that under such circumstances in *normal* persons the relative abilities of the myocardium to maintain the general circulation and of the coronary circulation to maintain the myocardium determine whether dyspnea or pain will be the predominant symptom In most normal persons dyspnea will be preponderant, but even in normal persons a third factor besides myocardial and coronary reserves, namely nervous sensitivity must be taken into account as modifying symptoms or exaggerating one or another especially precordial pain, palpitation, or faintness. *Hypersensitive* individuals in whom the effort syndrome is easily induced are likely to develop the same symptoms on excitement as on exertion at such times the symptoms form an excitement syndrome and not an effort syndrome.

The effort syndrome, though easily induced, might be considered at first thought to be unworthy of any special discussion since, so far as we know it is not an organic disease, and since it may occur in perfectly normal persons but when it is of high degree, that is, when it is very easily induced and the symptoms are marked, it is important for three reasons. In the first place, it is itself often a partially or completely incapacitating condition. Secondly proper treatment is very important and is often neglected. And, thirdly it is essential to distinguish it from organic heart disease or to recognize its presence when it complicates organic heart disease.

An abnormally high degree of effort syndrome has long been recognized, generally as but a part of a "neurasthenic" state, and it has so been labeled in medical practice. Occurring with great frequency among the British soldiers in India and among the Union soldiers during the American Civil War as the result of excessive strain and hardship, it was called the "excitable" or "irritable heart of soldiers" (Myers, 1870; DaCosta, 1871) DaCosta's classical account is the first good description of the condition and so deserves quotation here.

DaCosta, J M. "On Irritable Heart; a Clinical Study of a Functional Cardiac Disorder and Its Consequences. *Am. J M Sc.*, 1871 LXI, 17

"In this paper I propose to consider a form of cardiac malady common among soldiers, but the study of which is equally interesting to the civil practitioner on account of its intimate bearing on some obscure or doubtful points of pathology Much of what I am about to say I could duplicate from the experience of private practice yet I prefer to let this inquiry remain as it was originally conducted on soldiers during our late war The observations here collected were made on a series of upwards of three hundred cases.

"General Clinical History—The general clinical history of many of the cases was this —

A man who had been for some months or longer in active service, would be seized with diarrhoea, annoying, yet not severe enough to keep him out of the field or attacked with diarrhoea or fever he rejoined, after a short stay in hospital, his command, and again underwent the exertions of a soldier's life. He soon noticed that he could not bear them as formerly he got out of breath, could not keep up with his comrades, was annoyed with dizziness and palpitation, and with pain in the chest his accoutrements oppressed him, and all this though he appeared well and healthy Seeking advice from the surgeon of the regiment, it was decided that he was unfit for duty and he was sent to a hospital, where his persistently quick acting heart confirmed his story though he looked like a man in sound condition. Any digestive disturbance which might have existed gradually passed away but the irritability of the heart remained, and only very slowly did the excited organ return to its natural condition. Or it failed to do so, notwithstanding the use of remedies which control the circulation, thus the case might go on for a long time, and the patient, after having been the round of hospitals, would be discharged, or as unfit for active duty placed in the Invalid Corps.

"Causes.—In discussing the causes we are led to examine some of the most interesting questions connected with this inquiry But in no part of it is it more difficult to arrive at fixed conclusions, for many causes seem at times to have combined and it is scarcely possible, even by the most rigorous analysis, to fix specially upon one. In the subjoined table great care has been exercised to arrive at the probable causing element. The cases which have served as its basis have been only so far selected that doubtful or ill-marked ones have been excluded, and that those patients who were chosen, were for the most part in good general health.

Analysis of 200 Cases

"Fevers	34	17 per cent
Diarrhoea	61	30.5 per cent
Hard field service, particularly excessive marching	69	34.5 per cent
Wounds, injuries, rheumatism, scurvy ordinary duties of soldier life, and doubtful causes	36	18 per cent
	200	100

"But in looking further and in endeavouring to explain the *nature of the malady* there is room for much doubt and difference of opinion.

"Treatment The treatment is never a short one and the question arises, would it not be better for the government at once to discharge these heart cases? I think not. The very worst ones, *those which after some months of treatment show*

no decided improvement had better be discharged. Until I understood the malady I retained the patients a long period in the hospital, later in the war a short time sufficed to make the proper disposition of them.

And from a military point of view further it enforces the lessons, how important it is not to send back soldiers just convalescent from fevers or other acute maladies, too soon to active work; that recruits, especially very young ones, be as far as practicable exercised and trained in marches and accustomed to fatigue before they are called upon to undergo the wear and tear of actual warfare; and it exhibits some of the dangers incident to the rapid and incessant manoeuvring of troops.

Rediscovered as a common military disorder in World War I this state of ill health was called the "soldier's heart," disordered action of the heart," and later "effort syndrome." The term "neurocirculatory asthenia" was finally employed in this country (Oppenheimer and associates, 1918) and this remains at the present time the most satisfactory designation, because it expresses its abnormal character by referring to both neurasthenic state and circulatory symptoms, and at the same time it does not limit the term to effort" or "irritability" or "soldier or make it too general by calling it by the vague inclusive designation "cardiac neurosis." It is simply one type of cardiac neurosis or of irritability of the heart, it occurs in civilians as well as in soldiers, it results from excitement as well as from effort, and it is not a normal response to ordinary effort. Also its symptoms are not exactly like those produced by effort in a normal healthy person.

Frequency It is impossible to state accurately the frequency of neurocircula tory asthenia for several reasons. The borderline is very wide and indistinct, and where the normal response ends and the abnormal response begins, especially with such variable factors as human individuals, it is impossible to say Moreover a normal person may have the condition for a short time during or after an acute illness or especial fatigue, without its being par ticularly noted by patient or doctor And, finally it has been included by most practicing physicians as a part of the more general terms "neurasthenia," "nervous prostration," and "neurosis.

It is possible, however to estimate roughly its frequency when well marked. Although common enough in civilian life, it is far less frequent and less severe than in the army in wartime. Lewis (1940) stated that during World War I sickness imputed by medical officers of the British Army to disturbances of the cardiovascular system was a chief malady one such case being numbered for every four cases of wound, following "chest" complaints as the second largest group of medical ailments. Five out of six of those "cardiac" cases suffered from neurocirculatory asthenia. After the World War of 1914–1918 there were 44 000 British soldiers who were pensioned for neurocirculatory asthenia. In World War II the condition cropped up in prominent degree in only the most strenuous campaigns, but in mild form it was encountered in many psychoneurotic soldiers undergoing their training in camps at home.

Of a series of 3 000 civilian patients with cardiac symptoms or signs who sought medical advice both in hospital and in private practice in New England (White and Jones, 1928) 302, or 10 per cent, were found to have neurocirculatory asthenia alone and 62, or 2 per cent more, showed well-marked neurocirculatory asthenia complicating organic heart disease, over half of such disease being of rheumatic type and another quarter of hypertensive type. Nearly 3 per cent of 2,314 cases of organic heart disease showed definite neurocirculatory asthenia. *A more recent analysis of 5 000 private patients with cardiac symptoms or signs seen by myself has revealed* 687 (13 7 per cent) with definite neurocirculatory asthenia, 448 (65.2 per cent) of these were uncomplicated by organic heart disease, 135 (19 6 per cent) were so complicated, and in the remainder (104 or 15.2 per cent) there was doubt about the presence of organic heart disease. Among the cases of organic heart disease found with neurocirculatory asthenia (a total of 4 7 per cent of the organic heart cases) rheumatic heart disease was most frequent (44 4 per cent) coronary heart disease was second (21 4 per cent) and hypertensive heart disease was third (18 per cent) there was only one case of cardiovascular syphilis.

The victims of the disorder are physically unfit, as it were chronically out of condition, unable to maintain any degree of physical effort, and quickly accumulating respiratory inefficiency and an excess of lactic acid on exercise.

Etiology *Cause* The cause of neurocirculatory asthenia is not known. The symptoms suggest that it may be a disorder of the autonomic or vegetative nervous system, a true neurosis not necessarily a psychoneurosis, but, even if it is, we are as yet unaware of its pathogenesis. The fundamental origin of the irritability and fatigability of the nervous system in so-called neurasthenia is still obscure these have usually been called functional disorders but the mechanism of such disorders is as yet unexplained. Abnormalities of central nerve cells induced by fatigue in experimental animals have been noted and may be possible factors. Moreover why gastrointestinal symptoms are most prominent in some neurasthenic patients, cerebral symptoms in others, and cardiovascular (neurocirculatory asthenia) in others has not been explained; variations in innervation or early accidental association with other troubles (indigestion, headache, extrasystoles, or cardiovascular symptoms on exertion) may be the answer We can only say now that in some patients neurasthenia manifests itself preponderantly by circulatory symptoms, and that neurasthenia itself is a disorder commonly found in certain individuals, usually under especial strain, who are equipped with a particularly sensitive nervous system.

Age Neurocirculatory asthenia is commonest in young adults, but it may occur at any age after early childhood it appears to be very rare in young children and it tends to decrease in incidence after early adult life. Of the 365 cases of this condition in White and Jones series, over half were between twenty and forty years old, 23 9 per cent being in the third and 27 4 per cent in the fourth decade of life. In the second decade 7 4 per cent were found

After the age of fifty years there were still a moderate number of cases—15.3 per cent. In war time among the soldiers the great majority of cases were *found in the third and fourth decades*, doubtless because such age groups made up the bulk of the soldiers.

Sex. Females are affected more often than males. The ratio in the series of White and Jones was 59 per cent female to 41 per cent male.

Heredity One of the most fundamental etiologic factors is that of heredity It is common to find that the close relatives and recent ancestors of patients with neurocirculatory asthenia have also had sensitive nervous systems, having suffered perhaps from this very same condition in the course of "nervous prostration or other such trouble. Recent studies have suggested that neurocirculatory asthenia belongs to the Mendelian dominant group of inherited disorders (Wheeler et al., 1948)

Strain. Besides heredity the one other etiologic factor of greatest importance is that of strain. This may be the result of worry over business, social, or family troubles, emotional conflicts, physical or nervous fatigue or both (as in the war) insomnia, exhaustion from acute infection or other illness, or undernourishment.

The toxic effect of tobacco alcohol, tea, coffee, and other substances does not itself cause neurocirculatory asthenia, although it may aggravate or perhaps even precipitate it. During World War I (1914–1918) it was thought that overindulgence in these things, particularly in tobacco and alcohol, might explain the great frequency of neurocirculatory asthenia, but actually the reverse was found, namely that the victims of this disorder realizing their sensitiveness, indulged in these things less than did the average soldier for otherwise their symptoms were often aggravated.

Other possible fundamental causes of neurocirculatory asthenia that have been suggested during the past 25 years are thyrotoxicosis, low-grade active infection, adrenal hyperactivity hyperventilation resulting in alkalosis, and salt lack, but none of these possible factors have been confirmed. All these conditions may precipitate or aggravate the symptoms of neurocirculatory asthenia, but they do not seem to be the fundamental cause. Hyperventilation combined with an anxiety neurosis is the nearest approach to the answer to date, the neurosis causing in some unknown way a sighing respiration with hyperventilation, the latter inducing in its turn faintness, dizziness, palpitation, and precordial discomfort.

Pathology There are no known pathologic changes in neurocirculatory asthenia. The heart as a rule is structurally normal, although there is sometimes associated organic disease No lesions of the nerves or of the glands of internal secretion have been found.

Symptoms. The symptoms of neurocirculatory asthenia are usually like those of effort syndrome in normal persons. In cases with lesser degrees of neurocirculatory asthenia the symptoms are not only relatively mild but they are fewer in number and in only the pronounced cases are all the classical symptoms present—dyspnea, palpitation, precordial pain and tenderness

faintness, dizziness, tremor sweating, and nervousness. In a series of 100 cases of neurocirculatory asthenia the four cardinal symptoms, namely palpitation, respiratory discomfort, precordial pains or aches, and exhaustion, were of *almost the same frequency varying in the order named from 78 to 73 per* cent (Craig and White, 1934)

The dyspnea is mostly subjective, there being an unpleasant consciousness of the ordinary respiratory act without much of any evident labor distress, or rapidity of respiration (a "breathing trouble," often in spells) sometimes there is a tachypnea, and during World War I cases were noted with an extreme but temporary acceleration of respiratory rate even to 100 or more per minute. *An interesting and commonly associated phenomenon is the abnormal increase of a tendency to sigh.* In fact the presence of abnormally frequent sighing is a helpful sign of the existence of neurocirculatory asthenia as differentiated from organic heart disease, for heart disease even in the presence of heart failure is rarely attended by sighing unless it is complicated by neurocirculatory asthenia.

The palpitation is for the most part simply the keen consciousness of the forceful action of the heart beating regularly and often rather rapidly arrhythmia is uncommon, but if premature beats or paroxysms of tachycardia do appear they usually aggravate the condition considerably and sometimes they set it off.

The precordial pain is as a rule a dull or heavy ache in the left breast, lasting for hours and not radiating, but occasionally it is interspersed with sharp stabbing sensations, substernal oppression is unusual though neurocirculatory asthenia may and in fact frequently does, complicate angina pectoris. When the heartache, or infrequently the substernal ache, is severe, it may radiate to the left arm and then be mistaken for angina pectoris still more easily Left breast tenderness is distinctive evidence of neurocirculatory asthenia.

The fourth prominent symptom, namely a feeling of exhaustion, present almost all the time but especially noticeable the first thing in the morning, is a striking characteristic in the great majority of cases of neurocirculatory asthenia. Not rarely it is the outstanding symptom. Other common symptoms —dizziness, faintness, and tremor—are present in varying degrees and indicate the instability of the nervous state and of the vasomotor control.

It is usually the combination of excitement, exertion, and fatigue that precipitates the maximum degree of symptoms in a susceptible individual and it is this combination in war times that occasions the great exaggeration of the disorder in so many nervous young soldiers. More or less incapacity results from marked neurocirculatory asthenia often more than that resulting from organic heart disease, and sometimes even complete disability ensues. It is a real and not an imaginary incapacity even though at first glance it may have appeared imaginary during World War I (1914–1918) when it was sometimes labeled "malingering," and even though in civilian practice it has frequently been diagnosed as "mere nervousness."

An important finding in neurocirculatory asthenia of high degree or easily induced, as in civilian life or in early milder training for war is the associated psychoneurosis of anxiety type. So common is this that the two conditions have sometimes been confused one for the other or considered to be synonymous, the term anxiety neurosis having come to mean for many the same collection of symptoms which identify neurocirculatory asthenia, although strictly one can be neurotically anxious about something without dyspnea, chest pain, or palpitation. Experience has shown, however that one condition can occur without the other as well as that either one can excite the other Nevertheless the close correlation is helpful in the weeding out of the more pronounced cases of neurocirculatory asthenia from the recruits for the armed services by the neuropsychiatrist who is particularly trained to pick out the psychoneurotics and those likely to become such.

Signs. The signs of neurocirculatory asthenia are general, the heart itself giving no evidence of trouble other than a tendency to increased force of action and sometimes increased rate, unless of course it happens to be the seat of organic lesions. A worried expression, tremor sometimes flushing, somewhat quickened respiration, and sweating are commonly found in a well-marked case. Special methods of examination such as blood pressure studies, roentgenology and electrocardiography reveal no particularly characteristic abnormalities in an occasional case, however the *T* waves in Lead 2 of the electrocardiogram may be temporarily flattened or even inverted, probably due either to a preponderant sympathetic nerve imbalance or to an unusually vertical position of the heart (so common in this type of individual of asthenic build) or to both these factors (see Chapters 2 and 9) The blood pressure may be a little elevated and variable. Strength and endurance tests and vital capacity usually show a subnormal value and are considerably reduced in marked cases; this fact weakens the value of such strength and vital capacity tests in judging the state of the heart itself An interesting abnormality is an easily induced oxygen debt on exercise, with excess accumulation of lactic acid. Another interesting finding is abnormality of shape of the capillary loops at the base of the nail in neurocirculatory asthenia (Cobb, et al., 1946) somewhat as has been noted in certain neurotic states.

Course and prognosis. The course of neurocirculatory asthenia is very variable, but the prognosis is always good so far as length of life is concerned, in fact better than the normal expectation (Wheeler et al., 1950) The degree of incapacity depends on several factors, chiefly on the intensity of the symptoms and on the adequacy of treatment. Recovery from a considerable degree of neurocirculatory instability is possible with care, but the patient is always likely to have a return of trouble if there is a return of the causative factors—infection, fatigue, worry and emotional stress. If these factors cannot be controlled, neither can the neurocirculatory asthenia be controlled. At the height of World War I it was suggested that this condition was but a forerunner of thyrotoxicosis or of heart disease or an accompaniment of infection, but none of these prophecies was fulfilled.

Of 558 soldiers with the condition reported by Lewis (1918) during World War I 286 (51 per cent) were found to be unfit for all military service, and of the remaining 272, 38 had to be removed from service later In civilian life complete incapacity is much less for two reasons (1) the degree of neurocirculatory asthenia is as a rule less marked in civilians, and (2) the strain of civilian life and work to which the patient must return is less than that of military service. Nevertheless it must be recognized that more or less complete incapacity can occur even in ordinary civilian life. However a follow-up study of 173 cases of neurocirculatory asthenia who had been examined by myself for the first time over twenty years ago has shown that the majority are still able to live a useful and reasonably comfortable life (Wheeler Reed, Cohen, and White, 1950)

A series of 601 war veterans with neurocirculatory asthenia was studied over a period of five years by Grant (1925) to determine the immediate prognosis of the condition. Of these cases 15 3 per cent recovered entirely 17.1 per cent improved, 56.2 per cent remained stationary and only 3.2 per cent became worse the remainder became ill or died from other diseases. The incidence of serious disease in the group was 8 7 per cent; the most frequent infection was pulmonary tuberculosis (3 7 per cent) The incidence of definite heart disease was only 1 per cent. The total deaths were but 14 (2.3 per cent)

So far as we know there is no tendency for patients with neurocirculatory asthenia either to die prematurely or to develop organic heart disease, but they often do live considerably restricted lives.

Complications. There are no particular complications of neurocirculatory asthenia, except the anxiety neurosis, although the condition may itself complicate any other trouble, such as infection heart disease, chronic illness of other nature, or trauma. Sometimes the symptoms of neurocirculatory asthenia, like other symptoms such as the palpitation resulting from paroxysmal tachycardia, lead to anxiety about them and establish an anxiety neurosis, and apparently vice versa thus, a vicious circle is easily established and is often hard to break.

Treatment. If fatigue, physical or nervous or infectious, is primarily or even secondarily responsible for neurocirculatory asthenia, rest is the important therapy for the moment and for as long—days, weeks, or months—as may be necessary adequately to counteract the fatigue. The rest, which may need at first to be complete, should be followed as soon as possible by a program of rehabilitation, re-education, and retraining. Reassurance at the start and in adequate doses afterward is often necessary but elaborate psychotherapy is generally not needed. In fact, since this condition is neither heart disease nor a mental disorder both cardiologist and psychiatrist are well kept away after the diagnosis has been established, so that the patient may not develop unnecessary fears about either heart or mental state, unless complications make the presence of such consultants advisable. It is essential at the outset in cases of neurocirculatory asthenia to rule out exciting factors, such as infection and important psychoneuroses, that in themselves need treatment.

One of the prime essentials in the treatment of neurocirculatory asthenia is to take the patient wholly into one's confidence, to explain fully what the situation is so far as we know it, and to dispel any fears of heart disease or death. The condition must be discussed seriously not lightly as if it were of no importance. It is just as wrong to regard the whole trouble as negligible or imaginary as is so often done, as it is to regard it as a dangerous or serious state which may threaten life and which demands rest in bed. Equally pernicious are the two extremes of diagnosis (1) "myocarditis" or cardiac insufficiency" and (2) "no disease" or imaginary trouble." A careless disregard of the disorder with hasty reassurance may make as much of a permanent cripple of the patient, who perhaps consults the advice of charlatans for their sympathy after being rebuffed by the regular medical profession, as does a grave face with the order to go to bed and to take digitalis. A half hour or an hour spent in full explanation at the onset of trouble, or at least at the first medical consultation, and a clear outline of treatment may save many days, weeks, or even years of invalid existence and hundreds of dollars spent on all kinds of doctors and medicines. So much good can be done in this way that too much emphasis cannot be placed on this method of procedure: it is often more fruitful and may need more skill and understanding than the treatment of a dozen cases of true heart disease.

The plan of life of the patient is to be worked out with care. Usually normal but quiet work and play are to be advised, with avoidance of late hours, coffee, tea, overindulgence in alcohol and tobacco, strenuous vacations, excitement in general, too many hours at work, and new and burdensome tasks or duties. Often the patient himself is aware of this necessity but he has perhaps disliked to humor his symptoms or to fall behind his fellows in strenuous living in the business, professional, and social world. With clear medical advice, however he realizes the wisdom of doing so and gradually he adjusts himself to suit his symptoms, and is surprised at recapturing a feeling of well being. After the preliminary talk a few further visits to the doctor may be all that are necessary to establish a satisfactory cure, without the need of a single drug or a visit to some expensive sanitarium. Symptomatic therapy for headache, insomnia, or extreme nervousness with bromides or hypnotics may be helpful but should be discontinued as soon as possible to avoid toxic effects and habituation. Digitalis generally makes the condition worse by increasing the force of the heart action or by producing toxic symptoms like anorexia.

Thus, rest, reassurance, and re-education are the keynotes of the therapy but after the condition is well established and has been wrongly treated for several years it may be very resistant to improvement, and some cases fail to respond to even the most enlightened treatment of the day

Attempts have been made at more or less specific therapy by attacks on certain conditions that have been thought to underlie or at least to accompany neurocirculatory asthenia, but these measures have not proved of value or are still in the experimental stage: they include denervation of the adrenal glands, the administration of sodium chloride, various vitamins and other

drugs, and intensive psychotherapy We still await a specific cure for routine use.

Differential diagnosis. The three conditions from which neurocirculatory asthenia at first glance may be sometimes difficult to differentiate are true heart disease thyrotoxicosis, and psychoneurosis. The absence of cardiac enlargement, of characteristic murmurs of valvular disease, of hypertension, of signs of heart failure, of angina pectoris or of abnormalities of roentgen ray shadow and electrocardiogram indicates at once that heart disease is not responsible for symptoms or incapacity Before the valuable experience of World War I (1914–1918) young adults, especially women, with uncomplicated neurocirculatory asthenia were occasionally wrongly diagnosed mitral stenosis because of their forceful heart action and of the unfamiliarity of the medical profession with the syndrome of neurocirculatory asthenia, now such errors are rarely made.

The absence of exophthalmos, of thyroid gland enlargement, and of abnormally high basal metabolic rate (carefully measured and judged) rules out thyrotoxicosis.

The most difficult differentiation of all is between neurocirculatory asthenia and psychoneurosis, particularly of the anxiety type. This is true because of the frequency with which one is engrafted upon the other probably much as neurocirculatory asthenia is a common accompaniment of infection though the reverse is not true. Since in the easily induced severer grades of neurocirculatory asthenia the anxiety neurosis is almost constantly found, there is little or no point in differential diagnosis in this respect in such cases, but in other patients more resistant to the condition it may be of considerable importance to distinguish the other exciting factors, namely physical exhaustion, nervous strain, and infection from the anxiety neurosis itself It is probably best, until we know more about it, to regard neurocirculatory asthenia as a disorder of the autonomic or vegetative nervous system that is, as a neurosis, in contradistinction to a psychosis or psychoneurosis.

The absence of fever or other evidences of infection indicates that neurocirculatory asthenia is not an immediate accompaniment of infection. Finally the recent history of nervous strain, fatigue, or infectious disease in an individual with a sensitive nervous system helps to establish the diagnosis of neurocirculatory asthenia.

PSYCHONEUROSES AND MENTAL DISORDERS

Any psychoneurotic state may have cardiovascular symptoms associated with it or be in part or completely based on a fear or a delusion of heart disease, even with no symptoms whatever This is very different from neurocirculatory asthenia where symptoms may be marked but where there may be no fear or delusion at all. In some cases the two conditions may be combined, as I have amply noted in the earlier part of this chapter

Heart symptoms or signs should be considered in their true light with relationship to the nervous disorder and specifically treated only if there is congestive failure, angina pectoris, or some such condition which can be definitely benefited, such treatment if indicated may itself result in improvement of the nervous disease and reinforce psychiatric therapy

Mental disorders and nervous instability may be initiated or aggravated by the fatigue or poor cerebral circulation resulting from actual heart disease and failure, generally in individuals in whom such mental or nervous trouble is rather easily induced In such cases satisfactory results from cardiac therapy so far as the heart and general circulation are concerned, usually improve also the nervous and mental state, but may not cure it. Mental disorders and nervous instability that are brought to light by heart failure or by cerebral anoxia of other cause, such as congenital heart disease with venoarterial shunt, are simply latent troubles that tend to recur under other strains than heart failure and often progress to a permanent state of mental or nervous derangement. A psychosis resulting from too much digitalis has been reported but not confirmed It is almost certain that such a psychosis is precipitated by faulty circulation rather than by the drug. It is true however that sedative, hypnotic, and narcotic drugs given to cardiac patients may induce acute psychoses as they may in patients with other diseases or indeed in normal persons In such cases paraldehyde (2 to 3 drachms, 8 to 12 cc, by mouth, by rectum, or intramuscularly to be repeated in three or four hours if necessary) is the best hypnotic though not infallible. Acute psychoses have been temporarily induced in some patients rapidly dehydrated by vigorous diuresis.

Hypochondriasis is a fairly frequent disorder and, so far as the heart is concerned, may be based on the occurrence or belief of the occurrence of heart disease in other members of the family or in friends, with fear of development of similar trouble in the individual himself, or on a slight symptom like palpitation from a premature contraction, or on mild neurocirculatory asthenia (effort syndrome) or finally on the knowledge of the possession of a systolic murmur which may be wholly unimportant. It may be a very distressing condition, difficult to treat and requiring the aid of a psychiatrist, or on the other hand it may be controlled easily by careful examination and reassurance.

Hysteria may assume a cardiac phase without either symptoms or signs of cardiac nature. After cardiovascular examination the treatment of the underlying psychiatric disorder should be turned over to expert hands.

Schizophrenia (dementia praecox) may be associated or aggravated by heart disease, as in a patient of my own with congenital patency of the ductus arteriosus of high degree, with intense continuous "machinery" murmur and thrill, who constantly reiterated her displeasure at having within her a woman who plotted against her with a roar of machinery Schizophrenia is, however infrequently associated with heart disease and the protected life of its victims seems to guard them from early onset of the so-called degenerative types of heart disease. Special shock therapy as by the use of Metrazol or electricity for this

or other psychoses, rarely if ever hurts the normal heart except for the induction of temporary disturbances of rhythm in some cases; slight unimportant changes in the electrocardiogram have also been noted.

General paresis, a disease of the central nervous system due to syphilis, is frequently complicated by syphilitic aortitis. It has been estimated that about 20 per cent of these paretics are so affected.

Senile dementia is often attended by coronary heart disease, in keeping with the widespread arteriosclerosis that is present, but the sheltered invalid existence renders the prognosis better and symptoms fewer than in the average individual with coronary heart disease. On the other hand the mental state may render the diagnosis and treatment of angina pectoris, myocardial infarction, and early stages of congestive heart failure difficult or in some cases impossible, as indicated by the significant finding of cardiac rupture in a majority of cases (16 out of 22) of myocardial infarction in the Massachusetts State Psychopathic Hospital; only 2 of the cases had been diagnosed as coronary occlusion during life (Jetter and White, 1944).

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CHAPTER 23

OTHER ETIOLOGIC FACTORS AND RELATIONSHIPS

Neoplasms. Among the rare and relatively unimportant causes of heart disease are cardiovascular neoplasms. It is doubtless because of their rarity and pathologic interest that they have been so often reported in the medical literature. All kinds of tumors, both primary and secondary including malignant lymphoma (Hodgkin s disease, lymphoblastoma) have been found in the heart and pericardium. Metastases from malignant disease elsewhere are much more numerous than primary malignancy Mahaim has written in recent years (1945) an authoritative book on the subject of cardiac tumors and polyps.

Primary tumors of the heart have been reported to occur about once in 2,000 cases that come to necropsy (0.05 per cent) 75 per cent of such tumors are benign (Lymburner 1934) On the other hand metastatic malignancy of the heart and pericardium has been discovered in 118 out of 11 100 consecutive cases autopsied at the Cleveland City Hospital from 1919 to 1939 (1 1 per cent) these metastatic malignancies involving the heart and pericardium made up 10.9 per cent of the 1 082 cases of malignant disease in the whole series and were especially common with carcinomas of the bronchus and of the breast which were found in 48 per cent of the cardiac and pericardial cases (Scott and Garvin, 1939) In another series metastatic lesions in the heart were discovered about once in 200 cases of malignant disease elsewhere in the body (0 6 per cent) (Lymburner 1934) Of primary tumors there have been reported, in the order named, most commonly myxoma, sarcoma, and rhabdomyoma, less often carcinoma, fibroma, lipoma, angioma, cystoma, papilloma, teratoma and epicardial epithelioma. In 1922 a review of the literature revealed the record of 150 cases of primary tumor of the heart, 40 of which were sarcomas a new case of primary sarcoma was reported then (Goldstein) During the next 25 years over 50 more cases of primary cardiac tumor were reported, including myxoma, carcinoma, sarcoma, and xanthoma. The new case of primary sarcoma of the heart reported by Wier and Jones in 1941 raised to 76 the total number of such tumors then on record. More cases

were added in 1948 (Shelburne' Halhuber and Kapferer) and a primary sarcoma of the abdominal aorta has also been reported (Nencki, 1946) In a reported series of 3 000 consecutive autopsies there were no primary heart tumors but there were 6 cases of secondary cardiac neoplasm, originating twice in the uterus and once each in rectum, kidney gallbladder and lung (Thorel 1903 1907) this illustrates not only the preponderance of secondary cardiac



FIG. 117 Metastatic melanotic sarcoma showing many lesions throughout the myocardium of both ventricles and septum of the heart. (Kindness of Dr Pedro Castillo, H vana, Cuba.)

tumors but also the multiplicity of the original tumor sites. Among cardiac metastases malignant melanoma (Figure 117) has held a prominent place, 4 cases having been added in 1939 (Moragues) to the 23 on record, and at least 5 more have been reported since (Raven, 1948 Lefkovitz, 1948 Ritz, 1949) A recent report of 30 cases of metastatic cardiac tumors has been published by Piotti (1949) consisting of 23 carcinomas and 7 sarcomas in 17 men and 13 women, the diagnosis was correctly made ante mortem in 20 of the cases. Eight of the primary tumors were bronchial (6) or pulmonary (2) Tachycardia was the most common sign.

Primary sarcoma of the pericardium has been reported in 11 cases, 10 collected in 1931 (Yater) and one added later (Steuer and Higley 1935) Metastatic pericardial malignancy secondary to a lung tumor may be very

extensive (Figure 118) Bloody pericardial fluid is commonly found in malignant disease of the pericardium.

Any heart chamber may be the site of neoplasm whether primary or secondary but the right chambers are more often involved than the left, doubtless because the tumor is so often spread by the blood stream (Lymburner 1934) even the node of Tawara can develop its neoplasm (Mahaim, 1942)

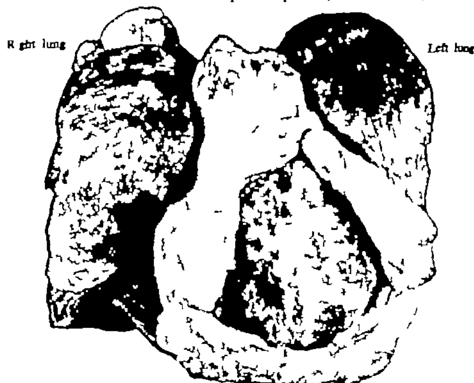


FIG 118 Photograph showing extensive malignancy (carcinoma) of the pericardium secondary to tumor which is visible at the apex of the right lung. The heart is somewhat compressed by the massive cancer surrounding it. (Kindness of Drs. Tracy Mallory and Benjamin Castleman, Massachusetts General Hospital, Boston.)

Only rarely has it been possible to diagnose neoplasms in the heart before death in the past, but that is changing now as noted in Piotti's report above. As a rule they are relatively unimportant metastases or primary growths discovered incidentally at postmortem examination in persons dying of malignant or other disease elsewhere than in the heart. In rare cases they may weaken the heart wall or produce heart block (atrioventricular or intraventricular) or other arrhythmias, or embarrass the circulation otherwise by their size, causing cyanosis and even simulating valvular disease by obstructing the valve ostia hence in heart trouble of unknown cause they should be thought of and looked for clinically Roentgen ray examination (showing unexpected heart size and shape) the discovery by electrocardiogram of atrioventricular or bundle branch block or *T* wave changes not otherwise explained, the find-

ing of a pericardial friction rub or effusion apparently not the result of infection, and the presence of neoplasms elsewhere afford the most suggestive evidence. The prognosis is serious except in the case of a few benign tumors, and yet as a rule the individuals affected die of other than the cardiac involvement. There is at present no adequate treatment for cardiac neoplasms surgery radiotherapy and chemotherapy of the tumor cells have not yet been sufficiently developed, although life may be somewhat prolonged by radiotherapy in certain cases, especially in those of malignant lymphoma.

Poisoning other than by infections. The effect of infectious toxins on the heart has already been discussed, there remains the consideration of the effect of other poisons or possible poisons. Fortunately any destructive myocardial effect of *heavy metals* as in arsenic, bismuth, and mercury poisoning is very rare, and fatal results come, as a rule, not from the cardiac involvement but chiefly from the damage to other organs, in particular to liver and kidneys. Mercury now in very common use as a diuretic, has been surprisingly well tolerated, but in rare instances it has caused renal damage and, in nearly unique cases, collapse or sudden death of uncertain (perhaps cardiac) nature. Phosphorus poisoning may depress the *T* waves and the *S-T* segments (Dathe and Nathan, 1946) There has been no observation of direct injury to the heart in lead poisoning. *Illuminating gas* (carbon monoxide) has been reported to have caused necrosis in the myocardium and in the media of cerebral arteries of persons dying of its effect (Grunewald, 1926) and electrocardiographic abnormalities, such as a-v block (Almgren, 1946 Casolo, 1947) Certain other poisons taken as food have been found to influence the heart, for example, the mushroom *Amanita phalloides* has been reported to have been the probable cause of temporary right bundle branch block (Hyman, 1928) Central American snake venom has been noted to depress the *T* waves and *S-T* segments and to prolong the *Q T* interval (Garcia-Carrillo, 1947) and the scorpion's bite can cause tachycardia and arrhythmias (Celoria and Sloer 1948)

Drug poisoning The drug most likely to poison the heart is *digitalis* itself which is used so often to control heart failure. If given in excessive dosage, digitalis may easily irritate the heart, producing premature beats (extra systoles) atrioventricular block, sinoatrial block or even atrial standstill, atrial paroxysmal tachycardia, atrial fibrillation, ventricular paroxysmal tachycardia with or without alternation in direction of the ventricular complexes in the electrocardiogram, and in rare instances ventricular fibrillation and death. La Due (1947) has produced myocardial necrosis, fibrosis, and atrophy in 44 per cent of dogs which he subjected to daily intravenous doses of large amounts of digitalis. It is very helpful to follow electrocardiographically the administration of saturating dosage of digitalis, thus watching for some of the signs of poisoning, as indicated by excessive inversion of the *T* waves and especially of the *S-T* segments, by prolongation of the P-R interval (atrioventricular block) by the appearance of ventricular premature beats occurring bigeminally and if the poisoning is of dangerous degree by the onset of ven-

tricular paroxysmal tachycardia. Such electrocardiographic signs indicate that a considerable percentage of the lethal dose of the drug has already been administered. Other indications of digitalis poisoning should also be looked for namely anorexia, nausea, vomiting, and visual disturbances (cloudy or colored vision) Diarrhea is a less common toxic effect of the drug. The possibility of a deleterious toxic influence of digitalis on the heart is an important reason for not administering the drug carelessly Digitalis poisoning became more common in this country for a while on two occasions in recent years first, after the strength of American preparations was raised, some 30 to 50 per cent during the period of the eleventh edition of the *U.S. Pharmacopeia*, 1936 to 1942 (Bland and White, 1941) dropping since the publication of the twelfth edition in 1942 to a 16 to 30 per cent increase over the strength of the standard unit prior to 1937 and, second, when digitoxin began to be used more freely with large daily rations of 0 2 mg or more (see Chapter 30) Fortunately serious poisoning of the heart by digitalis given by mouth is unlikely to happen because of the emetic effect of large doses.

Quinidine sulphate another very helpful drug that may poison the heart, has been used considerably in recent years in the treatment of cardiac arrhythmia, particularly atrial fibrillation. This medicine may have a harmful effect on the heart as well as the beneficial effect of abolishing atrial flutter and atrial fibrillation. Such harmful effect is shown by the presence of sinoatrial depression, intra-atrial block, and intraventricular block, and rarely premature contractions, paroxysmal tachycardia (atrial or ventricular) and even ventricular fibrillation or standstill. It is probable that the rare cases dying suddenly during quinidine therapy have for the most part suffered direct fatal quinidine effects on the heart, in particular total standstill due to paralysis of both sinoatrial and atrioventricular nodes. The drug should be employed only with great care if large doses are administered, and then only under close observation with electrocardiographic control. Quinidine therapy will be discussed further in Chapter 33

Other drugs are less frequently the cause of heart trouble, although occasionally when one of them is given too vigorously such as *arsenic* in large dosage in the treatment of syphilis, heart failure may be precipitated. The *salicylates* including aspirin, may cause serious poisoning and even death in rare cases, which show postmortem petechial and larger hemorrhages scattered throughout the body and focal necroses (Krasnoff and Bernstein 1947)

The intravenous therapeutic use of *calcium* in high concentration can prolong systole, depress the cardiac pacemakers and conduction tissue (to cause bradycardia and heart block) and increase the excitability of the ventricular muscle (to produce ectopic beats) (Clark, 1941) *Potassium* in large dosage elevates the *T* waves of the electrocardiogram and widens the *QRS* waves, while tending to produce abnormal peripheral sensory reactions (paresthesia) it should be employed cautiously in renal disease since the poisonous concentration of potassium in the blood is a common occurrency in renal insufficiency (Thomson, 1939 Keith, et al., 1942)

Tarail (1948) noted that electrocardiographic changes begin to appear when the concentration of serum potassium lies between 6 8 and 7 6 milliequivalents per liter and are constantly found at amounts greater than 7.8 m.Eq /L. A fatal concentration in man is over 10 0 m.Eq /L. when diastolic standstill occurs with generalized flaccid paralysis (Finch, et al., 1946) Sodium and calcium salts, blood and glucose, may correct the effects when not extreme. Low potassium blood levels can also affect the electrocardiogram, flattening the *T* waves and prolonging systole.

Metrazol used to cause convulsions in psychopathic states, may induce extrasystoles of little import. *Ergotamine* raises and *adrenaline* lowers the *T* waves through their vagal and sympathetic effects respectively (Hartwell, et al., 1942) and *morphine* has long been known to produce vagal effects on the heart with slowing of the rate, delay in conduction, lowering of the *R* waves, and raising of the *T* waves (Einthoven and Wieringa, 1912) *atropine* neutralizes this effect and when given alone lowers the *T* waves (Hartwell, et al. 1942) Various other drugs may produce electrocardiographic changes, for example, *emetine* (for amebiasis) which lowers the *T* waves and delays conduction, and *antimony* (Fuadin and tartar emetic for schistosomiasis) which lowers the *T* waves and prolongs systole. The *sulfonamides* may cause myocardial necrosis in rare cases, but penicillin does not do so

Finally *chloroform* as an anesthetic has long been known to have a poisonous effect on the heart, causing extrasystoles and even ventricular fibrillation in animals, and probably by this same mechanism causing sudden death in rare instances in man chloroform and the newer related anesthetic cyclopropane are therefore far more dangerous anesthetics than ether and most other preparations, especially if the heart is already diseased and irritable.

There are a few substances used widely by mankind for pleasure or stimulation or because of habit that have as a rule but little deleterious effect on the heart; the literature is full of conflicting statements about their "harmless" or "pernicious influence. Such substances are alcohol, tobacco, tea, and coffee.

Alcohol in strong concentration and large amounts can perhaps injure the myocardium, but certainly to a far less extent than more sensitive organs like the liver and brain. In small or moderate amounts it has no harmful effect at all but rather a vasodilating action which relieves or prevents angina pectoris. Small quantities of alcoholic beverages through their relaxing effect may benefit individuals who are depressed or under nervous tension, and it is even possible that regular daily use of light wine or beer in moderation may favor the maintenance of good health. In fact it has been noted by several observers (Cabot, 1904 Leary 1931) that arteriosclerosis is rare in cases of excessive alcoholism suggesting a protective influence in that respect, though less than nothing is gained if liver brain, and morale are seriously damaged in the process. The cardiovascular reaction following acute alcoholism is, moreover often unfavorable, producing neurocirculatory asthenia, paroxysmal arrhythmias, increase in angina pectoris, or precipitation of congestive failure in

cardiac patients. Finally a considerable use of alcoholic beverages does not protect a person from serious coronary heart disease even in the forties, as I have found in the case of several patients.

Tobacco varies greatly in its effect according to the individual and also according to the tolerance produced by habit. It causes no actual heart disease but it may in large amounts or in susceptible persons, excite sinoatrial tachycardia, premature contractions, or paroxysmal tachycardia, and, in extreme cases, paroxysmal atrial fibrillation. Palpitation may be caused by these arrhythmias. In the majority of individuals, particularly hypertensive patients, the blood pressure (both systolic and diastolic) is raised appreciably and even the metabolic rate. In a few individuals with coronary heart disease the use of tobacco has been known to precipitate or to aggravate angina pectoris, and to cause tachycardia, temporary changes in the *T* waves of the electrocardiogram, and a harmful effect on the coronary circulation. In fact, in one healthy young man the inhalation of tobacco smoke has been observed temporarily to cause dizziness and inversion of the *T* waves in Leads I and 2 of the electrocardiogram so that they resembled for a few beats the *T* waves of coronary heart disease (Graybiel, Starr and White, 1938) whether this change is to be attributed to excessive sympathetic nerve stimulation, to coronary arterial constriction, or to a direct toxic myocardial effect we do not know but we are inclined to accept the first of these explanations. Various recent investigations (Roth, et al. 1944 Boyle, et al., 1947 Levy et al., 1948, Mathers, et al. 1949) have compared the effects of inhaling tobacco smoke with the injection of nicotine and have found them to be similar with increase of heart rate and blood pressure and lowering of the *T* waves of the electrocardiogram tachycardia is the simplest gauge of hypersensitiveness to tobacco (nicotine) Thus there is, after all, such a condition as a "tobacco heart," but it is a state of functional derangement of the heart and circulation and not organic heart disease. When the so-called denicotinized tobacco which contains only ⅓ to ½ or less of the amount of nicotine found in ordinary tobacco is used, the heart is much less likely to be disturbed in individuals who are sensitive to the plant. Tobacco also causes a peripheral vasoconstriction with lowering of the skin temperature (Weatherby 1942) and has been suggested as a factor in causing thromboangiitis obliterans, a disease of youth and middle age of unknown etiology to be discussed in Chapter 28 The chief disadvantage of tobacco in my experience has been the induction of cardiospasm and even gastritis as disagreeable complications in my cardiac patients or as trouble simulating the angina pectoris of coronary heart disease. Because of the fact that tobacco (nicotine) is, in most persons, a pressor agent it is wise to avoid its use in the presence of hypertension. Incidentally it is of interest that alcoholic beverages do not neutralize the vasoconstricting effect of tobacco (Roth and Sheard, 1947)

Tea and *coffee* do not cause heart disease, but by nervous stimulation they are frequently the cause of increased heart rate and palpitation, and, in some

susceptible individuals, of premature beats or paroxysmal tachycardia on the other hand, they may be helpful in cases of mild Cheyne-Stokes respiration.

A few years ago much excitement was engendered by the discovery of some *lithium* poisoning secondary to too liberal use of lithium chloride as a substitute for sodium chloride in low sodium diets, for congestive heart failure in particular Few serious cases were found among many thousands, but unfortunately this excellent taste substitute was largely abandoned whereas under proper control and in small dosage (e.g., a few drops of a 25 per cent watery solution amounting to not more than 0 05 gm a day) it is quite harmless and helpful. The symptoms of lithium poisoning are not cardiac, but include in particular weakness of muscles and mental confusion.

Finally *poisons may be generated in the body* itself to irritate or damage the heart. The most frequent well-marked example of this is in the case of uremia where abnormal heart action and distorted electrocardiograms have sometimes been found, doubtless the result of the toxic effect of the high content of potassium in the blood. Irritation of the heart as shown by the appearance of premature beats may sometimes be only a reflex nervous manifestation, which doubtless explains in large part the relationship of such conditions as indigestion, as well as of most focal infections, to cardiovascular symptoms. A slow pulse due to sinoatrial bradycardia, apparently a vagal effect, is occasionally prominent in cases of catarrhal jaundice the toxic effect of severe hepatic insufficiency is manifested especially by stupor and depressed respiration.

Disorders of nutrition. Avitaminosis. Obesity Fatty infiltration and fatty degeneration. Gout. Much has been said about malnutrition and the harmful effects of avitaminoses and much of it is true, but overemphasis on these conditions has had two harmful results (1) the excessive use of all kinds of expensive vitamin preparations, and (2) the relative neglect of overnutrition which, with or without obesity is doubtless more injurious to more persons than is undernutrition. It may well be that especially in the U.S.A. today overnutrition with its common companions diabetes, coronary atherosclerosis, and hypertension is on the way to becoming a major threat to the health of the people. An important consideration about malnutrition, especially the avitaminoses, is that the deficiency is only rare in one food element, whether protein, vitamin B_1 vitamin C, or vitamin D or other factor: the deficiency is almost invariably multiple.

Beriberi a disease which is primarily the consequence of vitamin B deficiency (tropical avitaminosis) has been shown to cause hydropic degeneration (intracellular edema) of the myocardium, particularly of the right ventricle, with cardiac dilatation and failure in rare cases. Electrocardiograms have shown in such cases small complexes, negative *T* waves in Lead 1 and slight aberration of the ventricular complexes. Beriberi was once a common disease in the Orient but it has been much reduced in the last generation by

change of diet from that of polished rice low in the essential vitamins, in the Occident beriberi has never been common but it is occasionally seen in severe alcoholism, in markedly restricted intake of food, as in Negro infants and young children reported by Waring (1929 1938) and in a few individuals with severe gastrointestinal disorders or psychiatric conditions resulting in semistarvation with avitaminosis. Heart disease with enlargement and peripheral vasodilatation with rapid blood flow are found complicating only the more severe cases of beriberi, often attended by a polyneuritis. Beriberi is one of the few conditions (another is arteriovenous fistula) which may result in congestive heart failure even though there continues to be an increased cardiac output (Weiss and Wilkins, 1937 Burwell and Dexter 1947) As a complicating factor in other conditions, especially in heart failure itself with poor appetite and malnutrition avitaminosis of mild to moderate degree may cause additional trouble and require specific therapy The edema of wet beriberi is largely the result of congestive heart failure but may also be favored by malnutrition with low serum protein. Relief is obtained primarily neither by digitalis nor by diuretics but by the administration of antineuritic vitamin B_1, intravenously in severe cases but by mouth with success in most patients.

Scorbutus (scurvy) due to lack of vitamin C, carries with it a tendency to hemorrhage which may involve the heart and pericardium as well as other parts of the body the heart muscle is said to show degeneration in scurvy

Rachitis (rickets) due to lack of vitamin D when very severe, is also associated with abnormality of the heart, consisting chiefly of dilatation and failure in a series of eleven children dying suddenly with rachitis each child showed at postmortem examination left ventricular dilatation (Meixner 1928)

Pellagra although an important and common deficiency disease, has not been found to be associated with any specific cardiac pathologic abnormalities except for changes in the *T* waves of the electrocardiogram (Rachmilewitz and Braun, 1944) circulatory troubles found in such cases are to be ascribed for the most part to lack of vitamin B_1 or to the hypoproteinemia of starvation, or to a coincident heart disease. Nicotinic acid is the specific treatment for pellagra, but all of the vitamin B group should also be given to cover the combined deficiencies present.

Starvation may cause generalized edema in victims of famine such edema may be the result of depression of renal excretion of sodium (Berkman, 1950) or caused by disturbed osmotic pressure due to low blood protein (albumin) as in cases of "nephrosis" and is not a manifestation of cardiac failure. The critical level of protein in the blood serum below which nutritional edema appears is about 5 gm per 100 cc the albumin-globulin ratio is often reversed. Adequate diet, especially rich in protein and vitamin B because of a frequently associated avitaminosis, quickly clears up this edema. Starvation decreases the heart size, cardiac rate and output, blood pressure, and electrocardiographic voltage, while increasing the duration of systole (Ellis, 1946 Simonson, et al., 1948) It has been estimated that for a loss of 30 per cent in body weight there is a loss of 20 per cent in the heart weight (Keys, 1948)

Obesity may or may not be attended by heart disease. It is common for obese individuals, because of lack of physical training and fitness and because of their excessive weight, to develop the effort syndrome easily but this does not signify heart disease It is, however now well known that obese persons have more hypertension and atherosclerosis and live shorter lives than do persons who are lean or of average weight, and yet overnutrition continues to be the rule in this country Most persons add 20 pounds or more of weight after the age of 25 years and such increased weight is due to the deposition of fat not just under the skin, but in the liver as well and in the coronary artery walls, it would seem to be common sense to avoid adding fat when there is already good nutrition.

There is a greater tendency also for obese individuals than for thin persons to store fat in and about the heart, especially in the interventricular and atrioventricular grooves and over the surface of the right ventricle into the musculature of which it may actually slowly penetrate, splitting the wall, and favoring atrophy of the myocardium and even rupture or failure of the right ventricle. Fat may be deposited subendocardially especially in the course of the atrioventricular conduction system, in an amount said to be sufficient to cause pressure and atrophy and, under special strain, even sudden death. Of these last mentioned effects of fat in and on the heart we have, however no proof.

Two common important sources of error in the estimation of heart size by roentgen ray arise as the result of obesity and fat deposits. In a stout person especially when there is much abdominal fat, the diaphragm tends to be high in position and the heart placed horizontally Such a horizontal heart shadow shows an increase above the average normal both in transverse diameter and in area (see Chapter 7) Hence a correction must be made in such cases in the estimation of heart size. When because of the horizontal heart position the transverse diameter approaches the long diameter in measurement (usually it averages 1.5 cm less) 1 to 2 cm may be subtracted from the transverse diameter and about 25 sq cm from the area in calculating the heart size. Also in such cases the aorta tends to be kinked by the upward pressure and looks much wider in the anteroposterior view than it actually is, sometimes resulting in an erroneous diagnosis of aortic dilatation. Views during deep inspiration and also with the subject in the oblique positions help to prevent errors of roentgen ray interpretation in obese individuals.

The other source of error in roentgen ray interpretation arises from the presence of a triangle of fat usually some 2 to 3 cm wide at the pericardial-diaphragmatic angle on the left just beyond the cardiac apex (Figure 7 shown on page 39) this is more common in, but not limited to obese persons. An extrapericardial layer of fat at the right heart border may also cast an appreciable and sometimes confusing shadow Unless care is taken the transverse heart diameter and the area may be erroneously measured and misinterpreted (McGinn and White, 1936)

That there is an actual *fatty heart (cor adiposum)* consisting of *fatty infiltration* as described above has been proved by pathologic studies but the

clinical significance of the condition is not clear· the truth probably rests between the two extreme views that the "fatty heart" is a common and dangerous condition and that it does not exist at all. Still more doubtful is the association of the cor adiposum with general obesity· they often are associated but there are also frequent exceptions, the fatty heart being found in the absence of obesity and obesity being found without the fatty heart. More study is needed to solve this problem.

Fatty degeneration of the heart may ensue in cases of marked fatty infiltration, but it is strictly a different condition and results as a rule more or less acutely from the toxic influence of infectious or noninfectious poisons, and from the cutting off of the blood supply to the myocardium by severe anemia (see below) or by the narrowing or occlusion of the coronary arteries. It is therefore not primarily related to obesity

Gout is often associated with excessive atherosclerosis and coronary heart disease which in the younger age group is frequently attended by an abnormally high content of uric acid in the blood, but there strictly is no such entity as a "gouty heart."

Blood diseases. Serious cardiac dilatation may occur with high grade *anemia* and may cause functional insufficiency of the mitral and of the tricuspid valves and in rare cases also of the aortic valve. In severe anemia of any type the circulatory rate is increased, with elevation of pulse pressure, stroke volume, minute volume cardiac rate and output, and oxygen consumption, and with decrease in the arm to tongue circulation time When the hemoglobin content drops below 25 per cent (3.5 gm) the cardiac dilatation may become extreme and congestive heart failure may appear without pre-existing heart disease In one series of 10 patients with very severe anemia (Tung, et al., 1937) 6 showed marked congestive failure with no other discoverable cause than the anemia. Treatment for and recovery from, the anemia usually results in a disappearance of the congestive failure and a return of the heart size toward or to normal. Anemia is one of the four important clinical conditions in which congestive heart failure is attended by an increased cardiac output, the other three being beriberi, thyrotoxicosis, and an arteriovenous fistula.

Electrocardiographic abnormalities are also common in severe anemia In one group of 76 anemic patients, 23 showed abnormal records (Szekely 1940) and in another of 45 cases, 10 had such electrocardiograms (Ellis and Faulkner 1939) The abnormalities consist of flattening or inversion of the *T* waves, depression of the *S-T* segments, and a tendency to low voltage of the *QRS* waves. With correction of the anemia the electrocardiogram usually returns to normal.

It may be concluded that the heart trouble in anemia is due to the combination of the myocardial anoxia and the increased work of the heart.

In *hyperchromic* commonly *pernicious anemia* years ago before the institution of specific liver therapy the heart was commonly found at postmortem examination hypertrophied and dilated with fatty degeneration of the myocardium in streaks farthest from the fresh blood supply that is, at the venous

ends of the capillaries, giving rise to a curious gross appearance which was called the "tiger" or "tiger-lily" heart. Although it was the anemia and not the heart trouble that was usually responsible for death, congestive failure and angina pectoris were seen in rare cases. Now that specific remedies have been introduced for pernicious anemia, protection of the heart has been possible against the changes noted above. In rare cases, however angina pectoris has apparently been precipitated during specific treatment of pernicious anemia, probably through the accompanying increase in blood volume.

Hypochromic ("secondary") anemia, if slight, has no deleterious effect on the heart, but if it is severe there may result the same fatty changes, dilatation, and hypertrophy that were at one time common in "primary" pernicious anemia. Also angina pectoris may occur in rare cases even in the absence of coronary disease (Elliot, 1934) Systolic murmurs at apex and base are common in severe anemia of any type, due to left ventricular dilatation with mitral regurgitation and to dilatation of the aorta and pulmonary artery Even diastolic murmurs, mitral and aortic and possibly even pulmonary are not rare in severe cases, the pathogenesis of such murmurs is undoubtedly concerned with the dilatation of the heart. With a much dilated left ventricular cavity and a rapid blood flow such as is usually found in marked anemia, a mitral diastolic murmur is produced by a relative mitral stenosis though the mitral valve itself is normal or even slightly dilated, while weakness of the aortic and pulmonary valve rings may result in their stretching with resulting regurgitation. Such murmurs tend to come and go according to the functional state of the heart. Gunewardene (1935) has called attention to the frequent wrong interpretation, labeled mitral stenosis, of cardiac dilatation in severe anemia in India.

In *sickle cell anemia* not only may the heart resemble the rheumatic heart with its enlargement and various murmurs but the course of the exacerbations of the disease over a period of years may resemble rheumatic fever the pains, however involve the long bones rather than the joints and are not relieved by salicylates (Klinefelter 1942)

With the reverse condition, *polycythemia* (or erythremia) the increased bulk of blood is an added burden for the circulation but strain on the heart is largely prevented by peripheral vasodilatation. The capillaries are uniformly found dilated in cases of polycythemia, whether primary (Vaquez-Osler disease) or secondary to congenital heart disease or chronic pulmonary disease. Vascular lesions, thromboses especially are occasional accompaniments of polycythemia, a study of 98 cases of polycythemia vera and of 35 cases of relative polycythemia by Norman and Allen (1937) revealed in about a third of the cases a variety of vascular complications—erythromelalgia, coronary thrombosis with myocardial infarction, angina pectoris, occlusive disease of the peripheral arteries, cerebral hemorrhage or thrombosis, intra-abdominal vascular thrombosis, phlebitis, and vasomotor neuroses.

Oxyhemoglobin may be limited in the blood by the existence of methemoglobinemia acquired as in the case of carbon monoxide or acetanilid poison-

ing or congenital as in the case of 5 members of one family reported by Gibson and Harrison (1947) It is important to distinguish the cyanosis in such cases from that of cardiac or pulmonary disease and from the reduced silver in the skin in argyria.

In *lymphatic leukemia* and less often in *myelogenous leukemia*, the myocardium, as well as many other organs and tissues of the body may be found *infiltrated with the abnormal leukocytes but this finding is merely a minor* part of these fatal diseases Hodgkin's disease (malignant lymphoma or splenic anemia) is discussed earlier in this chapter under the heading Neoplasms; it may be attended by severe anemia.

Trauma. Injuries of all varieties may involve the cardiovascular apparatus in any part—heart, pericardium, great vessels, arteries, or veins. Injuries of blood vessels are very frequent, and even trauma of the heart itself is not at all rare. There may be penetrating wounds of the heart by gunshot, bomb or shell fragments, knife, dagger sword, bayonet, or other instrument, such as were seen by the thousands during both World Wars. Injury may come indirectly by contusion from blows or falls, by crushing, or by intense jarring. Finally there may be spontaneous rupture" of valve cusp, chordae tendineae, papillary muscle, atrial or ventricular wall, or aorta. When rupture of any sort comes by indirect violence or spontaneously heart disease is usually found to underlie the injury—for example, bacterial endocarditis in the case of rupture of valve cusp or chordae tendineae, cardiac infarct in the case of rupture of heart wall, septum or papillary muscle (see Chapters 21 and 25) and aneurysm or medial necrosis in the case of ruptured aorta (see Chapter 28) Sometimes, however even when the trauma does not seem great, clean-cut rupture (usually linear tears) of heart wall or aorta may occur without any evidence of local disease at postmortem examination, such cases are to be explained by an unusual amount of strain exerted at the moment of full distention of heart chamber aorta, or valve cusp, the tissue in question being perhaps congenitally weak. A defect in the media of unexplained etiology (Erdheim, 1929—see Chapter 28) no doubt accounts for some aortic ruptures. The reports of proven cases show that serious or fatal injury can come even to a normal heart or aorta from indirect or direct trauma, as in striking the surface of the water in diving, without any penetrating wound. The greater the injury the more likely of course, is heart damage. See Figure 119 for rupture of papillary muscle.

Contusion or even partial rupture of the heart wall may also occur and because of the usual recovery of such cases may pass notice (Schlomka and Schmitz, 1932 Bright and Beck, 1935) A "steering wheel" injury produced by sudden compression of the anterior chest wall of the operator of a motor car by his steering wheel at the time of an accident is doubtless a cause of contusion of the heart (Bright and Beck 1935) but just how common it is we do not know there is considerable danger now of its exaggeration. In these days of claims for compensation for injuries by everything under the sun, the "steering wheel cardiac contusion" is having its share of publicity and has

already become the cause of at least some cardiac or traumatic neuroses. As a matter of fact the heart is a very mobile organ in the chest and is likely to escape injury whether the trauma is penetrating or not, in reviewing cases of wounds of the heart, Elkin (1938) noted that in his experience only 2 per cent of penetrating wounds of the chest injured the heart. Contusion or even rupture of the heart has been recognized as an occasional result of blast injuries resulting from bomb explosions in World War II or even as an industrial

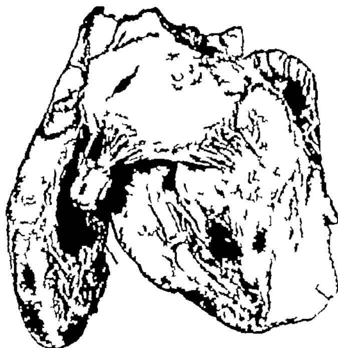


FIG. 119 Photograph of traumatic injury to the heart. Anterior papillary muscle of the left ventricle torn from its base (as shown by the arrow) in case of a young man run over by truck.

hazard (Miller 1947) The only clue to heart muscle contusion in some cases is electrocardiographic evidence of fresh myocardial damage: an electrocardiogram should be obtained whenever possible shortly after any severe thoracic injury Temporary changes, especially in the *T* waves, may follow a penetrating or contused lesion of the heart muscle and, like the electrocardiogram in acute myocardial infarction, aid in the localization of the damaged area.

In the last edition of this book (1944) I wrote that coronary thrombosis with myocardial infarction is not the result of trauma, so far as we know at present from the experience of many observers of many hundreds of cases, except in a few instances of advanced coronary atherosclerosis and narrowing to start with, and in others where because of an incised wound of the heart wall it has been necessary to ligate a major coronary artery in the course of

surgical repair Since then, however a case has been reported of a boy of ten years who succumbed to acute coronary thrombosis involving the left descending artery a few minutes after three rounds of a boxing match necropsy showed only slight atheromatous changes in the intima (Jokl and Greenstein, 1944)

In rare cases recovery may take place after rupture or penetrating wound of the heart, especially in the case of the latter injury if operative relief can be quickly afforded Many cases of successful healing of sutured wounds of the heart have been reported. There may be no sequelae after such wounds, and the heart, years afterward, may be found to be carrying on its function in a normal manner on the other hand serious after-effects may appear A striking case in a youth has been reported of perforation of the anterior mitral valve cusp (gunshot wound) producing pure mitral regurgitation and followed by enormous enlargement of the heart with hypertrophy and dilatation of all four chambers, and death after several years from congestive failure (Adam, 1927) In this last-mentioned case there was also an adherent pericardium following the hemopericardium produced by the injury but this had little or nothing to do with the cardiac enlargement and failure. Such a coincidental pericardial lesion may complicate any case of cardiac trauma. Another interesting instance is also on record of death from heart failure in the case of a young man 14 months after rupture, by a crushing injury of the cusps of his normal aortic valve (Kissane, et al. 1936) Heart block has been noted after cardiac trauma (Coffen, et al., 1941)

Successful suture of wounds of the aorta also has been proved possible, as in a case reported by Blalock (1934) and of vena cava too (Barnes, 1938)

One of the chief hazards of penetrating wounds of the heart is that of *cardiac tamponade from hemopericardium.* This may come quickly in the course of a few minutes or an hour or so and to the inexperienced eye may simulate shock. The pulse becomes small and rapid with very low pulse pressure and paradoxical character the neck veins become engorged (unless there is a coincident vascular collapse) because of their inability to empty into the acutely constricted or compressed heart, and death may ensue shortly unless surgical relief is afforded. The heart wall must of course be sutured to prevent further bleeding, but the emergency measure is paracentesis (or better incision) of the distended pericardium, as in a case reported by Rajasingham (1939)

Furthermore, *foreign bodies* may enter the heart wall or chambers and remain there, for years perhaps, with little or no harmful effect. Extraordinary instances have been reported of projectiles migrating to the heart by way of the great veins from distant wounds in thigh abdomen, or neck, and in two cases (Boeckel 1917 and LaRoque, 1926) of projectiles migrating from left ventricle and aorta respectively as emboli to block the femoral artery with resulting gangrene of the leg in Boeckel's case. Another very interesting case has recently been reported by Shapiro (1941) of migration of a hollow needle used for intravenous injection, from arm vein into the heart and through the

heart wall to lie eventually in the prepericardial fat between heart and diaphragm.

Trauma to the myocardium may result from excessive exposure to the roentgen ray This has been shown in experimental animals and found at autopsy in a few patients treated by radiotherapy for intrathoracic tumors. Clinical evidence of such injury has not yet, however been demonstrated convincingly

Arrhythmias are sometimes induced by trauma but as a rule they are unimportant, temporary and either subside spontaneously in the course of a few days or weeks or are easily controlled by treatment (see Chapters 32 and 33) this is true even of absolute arrhythmia (atrial fibrillation) which is likely to occasion unnecessary alarm, except in rare persons in whom congestive heart failure may be induced by the extra strain of the atrial fibrillation when there is already present chronic heart disease with limited reserve.

Electric shock whether accidental (Koeppen, 1940) or induced in the therapy of psychoses (Streat, 1941 Hejtmancik, Bankhead, and Hermann, 1949) can produce all kinds of disorders of the heart rhythm, but especially extrasystoles changes in the *S-T* segments and *T* waves have been reported, lowering of the former and at first elevation and later depression of the latter Electrocution results in death from (or with) ventricular fibrillation (following quickly after the appearance of extrasystoles and bundle branch block) (Kountz, personal communication, 1943)

Finally the question of the relationship of *occupational hazards* to cardiac trauma is important and often very difficult. Occasionally injuries received during work may traumatize seriously a perfectly normal heart, but as a rule heart symptoms or signs that follow industrial strain or accidents are either merely those of neurocirculatory asthenia or neurosis in sensitive individuals, or are due to the precipitation or aggravation of trouble in a heart already damaged or diseased. The decision as to the relative responsibilities of accident or strain and of previous heart disease in the production of symptoms and signs is often a great problem, sufficient to tax the wisdom of the most experienced physician or judge. A most interesting problem of sudden cardiac death on Monday mornings of employees of powder plants when hurrying back to work after being out of the nitrite atmosphere for some 60 hours during the weekend was a case in point (Drinker personal communication, 1935) this hazard was eliminated when the plants were adequately ventilated. Even after an adequate appraisal of the relative responsibilities of trauma or other strain and of pre-existing heart disease in the production of cardiovascular symptoms or signs of disability it is not always possible to adjust accident or industrial insurance compensation in accord, because of faulty local laws or regulations, that is, in some places the decision must be "all or nothing" instead of a proper percentage of the total. This faulty situation demands correction. Of the greatest importance in this connection is the value of careful routine (annual) cardiovascular examination of all industrial employees.

Thoracic and spinal deformities. An appreciable and sometimes serious handicap to the action of the heart and circulation may be occasioned by deformities of the thorax or spine, particularly marked *kyphoscoliosis*. The strain, however may be more pulmonary than cardiac with much diminished vital capacity of the lungs, but almost always both systems, respiratory and circulatory are involved with resultant pulmonocardiac failure (Chapman, Dill, and Graybiel 1939) The heart may be displaced (to the left with right scoliosis and to the right with left scoliosis) and deformed, and the great vessels compressed so that left ventricle or right ventricle or both may have increased work to do, with resulting hypertrophy and dilatation. Or the restriction of thoracic movement in respiration may result in special strain on the right ventricle such as occurs in the case of the cor pulmonale. In badly deformed individuals survival to old age is frequently prevented by the cardiovascular strain as well as by pulmonary complications.

Marked *depression of the sternum* (producing funnel chest or pectus excavatum) may in rare cases seriously embarrass the heart by flattening it anteroposteriorly and compressing the right atrium and right ventricle during expiration or by torsion of the great vessels usually however the heart is simply displaced to the left without any particular handicap unless the deformity is extreme with little mediastinal space between sternum and spine. Operative relief is difficult but may be successfully carried out as in the series of cases operated upon by Sauerbruch (Sauerbruch, 1931 O'Shaughnessy 1940) and as has been done since 1943 by Sweet at the Massachusetts General Hospital.

The presence of *cervical ribs* may occasion not only trophic disorders and disturbances of the peripheral circulation in the hands somewhat resembling Raynaud's disease and in some cases thrombotic and embolic obliteration of arteries of the arms and hands (Telford and Stopford, 1931 Eden, 1939) and even subclavian arterial thrombosis and hemiplegia due to cerebral embolism (Hoobler 1942) but it has also been thought responsible in some cases for disturbances of cardiac rhythm (premature beats, atrial paroxysmal tachycardia, atrial flutter) due to irritation of cervical nerves.

The *scalenus anticus syndrome* consisting of localized and radiating pain in and from the upper precordial and clavicular and shoulder regions and trophic disturbances in either arm, may simulate on occasion angina pectoris but it is usually readily differentiated by the longer duration of the pain and variation with a change in shoulder and arm position. It is caused by pressure of the anterior scalenus muscle or fibrous band representing rudimentary rib or middle scalenus muscle upon the subclavian artery (with reduction of pulse size and blood pressure) and lower portion of the brachial plexus It can be relieved by surgery with section of the offending structures (Rogers, 1941 Adson 1947) or by skeletal traction in selected cases (DePalma, 1948)

High altitude. Aviation hazards. Climate and weather *High altitude* increases the work of the heart in attempting to supply to the tissues an adequate amount of oxygen, the pressure of which in the inspired air is decreased be-

cause of the decrease of atmosphere at points much elevated above sea level. The influence of high altitude depends on several factors: first, the height above sea level; second, the individual's capacity to compensate for the oxygen decrease; third, the length of time the subject has lived at the high altitude; and, fourth, the degree of physical activity at this altitude. Below a height of 5 000 feet (about 1 700 meters) altitude has little or no effect; between 5 000 and 10 000 feet it probably has a slight to moderate effect; between 10 000 and 15 000 feet it has considerable effect; and over 15 000 feet (5 000 meters) it has a very marked effect on the circulation. Individuals vary greatly in their ability to adjust themselves physiologically to high altitudes and therefore in their ability to withstand *mountain sickness* which is due to low arterial oxygen saturation; the cause of the difference is not clear but it seems to depend, in part at least, on the capacity of the lungs to allow a rapid diffusion of oxygen from alveolar air to blood stream. Tests of this capacity of an individual to endure the low oxygen pressure of high altitudes, either on land or in the air, may be made at sea level without the expenditure of time and money necessary for traveling to very high altitudes. At an altitude of 15 000 feet the heart works about 20 per cent harder to accomplish 20 per cent less work than at sea level (Barcroft, and associates, 1922). An altitude of 10 000 feet is the more or less critical height above which mountain sickness is likely to occur. The more prominent symptoms of mountain sickness are headache, vertigo, nausea, dyspnea, palpitation, and weakness. The electrocardiogram of normal soldiers at 15 000 feet has shown elevation of *S-T* segments and inversion of *T* waves in several precordial leads corrected by descent to sea level (Alzamora and Monge, 1949).

Aviation medicine which has developed of late by leaps and bounds under the stimulation of modern warfare, includes not only the effect of high altitude as in mountain sickness, which can be successfully combated by the inhalation of oxygen, but also two other important circulatory strains, namely (1) that of the centrifugal force on the blood mass resulting from intense acceleration of the speed of modern planes and from abrupt change in direction, as in dive bombing, in part at least controlled by special equipment which compresses the lower part of the body and by prone body position, and (2) that of air embolism resulting from very rapid climbs to very high altitudes, requiring control by preoxygenation and denitrogenation or by the maintenance of a more or less uniform atmospheric pressure protecting the aviator. Very few cardiac deaths, however, have been recorded among several million passengers in air travel where the hazards are relatively slight (Graybiel, 1941). Of the greatest importance in the selection of pilots and other air crew is testing them for their ability to stand these various strains, since individuals vary greatly, and in maintaining them in a state of physical fitness.

Individuals who have lived long at high altitudes, for example 15 000 feet or more, acquire an ability not found in the newcomer to adjust the circulation to the low oxygen pressure. The adjustment expresses itself by the development of polycythemia, barrel-shaped thorax, and ability to undertake

relatively strenuous exertion which is impossible for the new arrivals. That the adjustment is not adequate is shown by the uniform occurrence of cyanosis, clubbing of the fingers, and pulmonary emphysema in the case of natives of very high altitudes (Talbott and Dill 1936) the lowest oxygen saturation of arterial blood in a series of six healthy workmen resident at 17 500 feet studied by Talbott and Dill (1936) was 67 6 per cent (normal 95 per cent) while the average in the six was 75 per cent and in ten temporary residents 76.2. Removal to low altitudes or the administration of oxygen is necessary to combat the excessive anoxemia that comes with an acute pulmonary disease like pneumonia. The degree of physical activity possible at high altitudes depends on the three factors already discussed even a native with good compensation is unable to perform at high altitudes an amount of work easily possible at low altitudes, without symptoms of circulatory distress (chiefly dyspnea and tachycardia) Heart failure is rare at high altitudes unless there is already serious heart disease. An increase in heart size, especially right ventricular in natives living at 4 540 meters has been reported by Rotta (1947)

In contrast to the effect of low oxygen tension in the inspired air high oxygen atmospheres (up to 50 per cent of oxygen) have shown no deleterious effects in the case of 2 normal men and 28 patients with cardiac insufficiency who were kept in such atmospheres for periods of time ranging from 5 days to 7 months, the patients were almost invariably benefited by such therapy (Richards and Barach, 1934) Pure oxygen at atmospheric pressure inhaled for many hours may produce pulmonary edema in animals but has been well tolerated and very helpful in human patients (A. L. Barach, personal communication, 1942) there has been no proof of depression of the respiratory center in the brain by prolonged inhalation of high percentage of oxygen except in rare deeply cyanosed cases with extensive pulmonary disease who require the aid of a respirator adequately to take in oxygen and to blow off carbon dioxide.

Very high atmospheric pressures may have harmful effects, as in caisson disease with its hazard of "the bends" due to gaseous emboli of nitrogen in blood and tissues (Behnke, 1940 Shilling, 1941)

Extreme variations in *weather* have an important effect in cardiac patients *in precipitating or increasing disorders of function such as congestive failure,* coronary insufficiency (angina pectoris) and arrhythmias. Intense cold, high winds, and excessive humidity are especially harmful but as yet little adequate study has been made on this important problem. In one series of cases attacks of coronary occlusion were found to be more frequent in winter than in summer (Bean and Mills, 1938) but in another series in New England (White and Bradl, 1935) the attacks were scattered quite uniformly throughout the months over a ten-year period Effort angina pectoris is certainly more common in cold weather but it is important incidentally to note that in intensely hot weather physical effort, which might precipitate cardiac symptoms, is normally reduced to a minimum

Work and exercise. Athletics. Physical work and exercise do not primarily cause heart disease or heart damage except in the rarest cases (see below) though they may precipitate or aggravate symptoms and signs of heart disease already present, and may temporarily exhaust the cardiovascular reserve even in a healthy individual. There has been much written about the "industrial heart" the "athletic heart," and the "military heart," but final conclusions cannot yet be drawn from the insufficient data that we possess. Suffice it to say that all three of these so-called heart conditions are nothing more nor less in most cases than fatigue or effort syndrome, especially marked in nervous individuals in whom it may amount to neurocirculatory asthenia. In some cases there may be also hypoglycemia and in others, who perspire much, lack of sodium chloride relieved by glucose and by common salt respectively.

Two other factors, however, are significant. One is real trauma due to exercise or work that may cause, either directly or indirectly, rupture of some part of the heart or great vessels, even when the heart is normal. The other is the possibility, in fact perhaps the likelihood, of actual increase in muscle bulk (hypertrophy) resulting from strenuous exertion continued for years. It is very difficult to decide this matter of hypertrophy. In the first place it is very rare to obtain postmortem data in the case of vigorous athletes who, while in normal health, meet a sudden accidental death. Secondly, slight to moderate hypertrophy alone may occur during life but not be particularly obvious on examination, even by roentgen study unless dilatation is also present. Thirdly, the range of the normal heart size is so great, even in individuals of the same height, weight, and age, that we have as yet no way of knowing whether or not in many cases there has been a change, even when we determine the exact heart weight post mortem; some more accurate correlation, probably with body build, than we possess at present is necessary, as already stated in Chapter 2, before we can draw definite conclusions. At present a very appreciable increase in size is possible in many cases without exceeding the outer normal limit. Finally, sufficient studies following the heart size of individual athletes or soldiers over many years have not yet been made. Some observations have been reported which suggest that slight enlargement of the heart is more likely to be found in professional ski runners, cyclists, and oarsmen than in other athletes. Also a few football players may have shown slight cardiac enlargement. However, even veteran marathon runners have failed to show enough hypertrophy to be evident by roentgen ray study. Cardiac enlargement, apparently largely dilatation, found in some athletes during their period of intensive sport, may subside when the athletic life is given up. The immediate reaction of heart size to vigorous exercise in an athlete is usually a diminution as shown by roentgen ray study, not to be accounted for entirely by a rapid heart rate.

It appears likely from the data that we possess at present that most hearts can endure great physical strain without difficulty and without enlargement but that a few react differently and eventually increase in size. It is quite possible that the chances of producing cardiac enlargement by physical strain

("the athletic heart") are greatest when four factors coincide (1) great physical strain, (2) rapid growth at adolescence, (3) temporary or chronic ill health, as from respiratory infection or anemia, and (4) unfavorable myocardial inheritance (to endure such strains) In most instances, however the circulatory system, including the heart, can in youth, and sometimes even at older ages, be brought to a high degree of efficiency and stamina, in athlete, soldier and laborer alike, by prolonged and skillful training.

It is of considerable interest to note that the hearts of very active animals are much larger than are those of relatively inactive animals of the same size; for example, the heart of the hare is three times as heavy relative to body weight, as that of the rabbit, while the heart of the racing greyhound is, in proportion to size, the largest mammalian heart of all (Herrmann, 1926) Finally when animals, such as dogs or rats, are made to exercise strenuously for long periods of time, it is found that eventually their hearts are considerably larger and heavier than those of control animals of the same age and size, and even from the same litter This is especially true when the strenuous exercise is imposed during the period of rapid growth. There is no indication that such hypertrophy when it does occur is harmful. Recent studies indicate that athletes do not suffer early disability or death because of their exercise in youth, in fact the reverse seems to be the case, at least as regards oarsmen (Cooper et al. 1937 Hartley and Llewellyn, 1939) An interesting volume was published by Morgan in 1873 entitled "University Oars, a critical enquiry into the after health of the men who rowed in the Oxford and Cambridge Boat Race from the year 1829 to 1869 based on the personal experience of the rowers themselves" these oarsmen lived longer and healthier lives than the average Britisher of their day Although it is true that it is the man of muscle (mesomorph) and therefore the athlete who is more prone than either ectomorph (thin) or endomorph (fat) to develop serious coronary heart disease in middle age (see Chapter 21) the oarsman is as a rule not built like the usually bulky mesomorph, that is, he is taller and more rangy and so may be less vulnerable to early coronary atherosclerosis. Much more study of all types of athletes in this respect is needed.

It is possible for a well-trained athlete to support a valvular lesion like aortic regurgitation if not marked, without symptoms, and be much more fit physically for the time being at least, than a person living a sedentary life whose heart is undamaged. In fact, in the absence of important symptoms exercise in moderation is beneficial for a person with chronic heart disease at any age because of its favorable effect on the peripheral circulation (reducing venous stasis and the hazard of thrombosis) pulmonary reserve general musculature, digestion, nervous system, and morale. It is wise, however in the long run, to limit considerably the strain of vigorous exercise on the heart when there is clear evidence of enlargement with or without valvular disease, especially during rapid growth in adolescence.

Military service. The problem of the selection of recruits for military service is a matter of recurrent interest and importance. What has been said above in

the last section on the effect of work and exercise on the heart and circulation (as well as in the previous section, on high altitude) has a direct bearing on this subject. The other points of importance concern the incidence of cardiovascular defects found in the young men of any given community or country and the relative size of the army and navy and air force required. When relatively small forces are needed, the physical standards for acceptance of the recruits can be kept at a high and rigid level, with only two classifications, namely fitness for full combat duty and unqualified rejection. Those accepted for service under these conditions should have no taint of suspected heart disease in the form of cardiac enlargement, murmurs of valvular defects, disturbing arrhythmias, overhigh blood pressure or pulse rate, or troublesome symptoms either of cardiac origin or of neurocirculatory asthenia nor should there have been a history of rheumatic fever pericarditis, or coronary heart disease. When, however there is a large expansion of military forces the bars must be let down, and not only the criteria for full combat duty made less rigid, but also a third classification adopted, namely of acceptance for limited service. During preparations in this country for World War II about 20 per cent of the candidates for military service were rejected for physical reasons and about 8 per cent of the rejections were for cardiovascular defects, ranking fifth in the list of causes for rejection after defects of teeth, eyes, nervous system, and ears, in that order The reasons for cardiovascular rejections varied greatly in different parts of the country but on the average ranged as follows in the order of frequency valvular disease, hypertension, neurocirculatory asthenia, and tachycardia. The chief difficulties concerned the upper limits of acceptable blood pressure and pulse rate, the interpretation of a relatively slight apical systolic murmur and the detection of men likely to develop neurocirculatory asthenia under too little provocation more studies were considered necessary to solve these problems which concerned not only fitness for service at the moment but also the future state of health after the war should end (Levy Stroud and White 1943) A follow-up study of men rejected during World War II for cardiovascular reasons has indicated that the only important problem that remains is that of the upper limits of acceptable blood pressure (White, et al., 1949)

After the recruit's admission to the armed forces his heart is likely to trouble him very little, since presumably it is normal to start with. He may acquire rheumatic fever and if he does he may have to be discharged from service, not so much because of any heart disease that may result (unlikely if not already present before examination as a recruit) but rather because of prolonged illness and liability to recurrence. Syphilitic aortitis with aneurysm or aortic regurgitation, once the typical "soldier's heart" and responsible for half of all the cardiovascular deaths in the British Army in the middle of the nineteenth century (Myers, 1870) has now been practically wiped out—only one death from aortic aneurysm occurred among 175,000 officers and men in the United States Army in 1937 Hypertension may develop among the older officers and men (Hillman, Levy Stroud, and White, 1944) The other current difficulties

of the present day seem to be neurocirculatory asthenia and the discovery by symptoms or electrocardiogram, of presenile coronary heart disease (White, 1941 1951) Coronary heart disease was diagnosed in over 800 men under the age of 40 years in the army of the U.S.A. during World War II, half of the diagnoses were confirmed by autopsy (Yater et al. 1948 see Chapter 21)

The problem of the airman s heart and circulation is a very special one. As perfect as possible at the time of selection the aviator needs chiefly to avoid staleness and to keep himself fit so that, with the aid of oxygen, he may avoid the hazards of anoxia and of centrifugal forces in flights at high altitudes, at high speeds, and with sudden changes in speed and in direction. Various tests, especially the Schneider Index (see Chapter 10) have been instituted to measure the fitness of pilots and other aviators, but not one of them is apparently as reliable as the close personal daily observation of the men by their own flight surgeon (Poppen, 1941)

Pregnancy Pregnancy augments the blood flow and it has been estimated that the work of the heart increases steadily during pregnancy to a level of about 50 per cent above that in the nonpregnant state (Stander and Cadden, 1932) It used to be thought that this maximum strain was at or just prior to full term, but it has since been shown that it occurs toward the end of the ninth lunar month, at which time "lightening" takes place, following which there is much less strain on the heart and hence less failure in cardiac cases in the tenth month (Cohen and Thomson, 1939) Another study has indicated that an important factor increasing the blood flow and the work of the heart in the pregnant state is the placental circulation, the effects of which resemble those of an arteriovenous aneurysm (Burwell, et al., 1938) There has been a difference of opinion as to whether or not the heart is enlarged for the time being because of this increased work or increase in blood volume. In advanced pregnancy it is difficult to judge the heart size because of the upward displacement of the heart by the enlarged uterus, which displacement incidentally is responsible for prominence of the Q waves and inversion of the T waves in Lead 3 of the electrocardiogram so often found during the latter half of pregnancy There probably is slight enlargement in pregnancy but it is clear that it is not great. One other general observation of circulatory interest in pregnancy is that the enlarged uterus tends to obstruct the venous return to the heart and to cause stasis in the leg veins.

Studies of pregnant women in this country have shown that about four per cent of all cases have heart symptoms or signs half of these have merely "functional" mitral systolic murmurs (probably associated with slight functional cardiac dilatation of little or no importance) or neurocirculatory asthenia the other half (2 per cent of all cases) have organic heart disease. In some places, Montreal for example, a lower incidence of heart disease (1 per cent) has been found (Campbell, 1923) in others it has apparently been much less (Schmidt in Bonn, 0 4 per cent for example) and in others somewhat more (Daly in Chicago, 2.8 per cent, Schaupp in San Francisco, 2.1 per

cent) More recent reports have given figures of 3 02 per cent (720 out of 23 858 pregnant women—Stromme and Kuder 1946) 3.2 per cent (203 cardiac cases of 6,285 consecutive pregnancies—Lease, 1948) and 0 8 per cent (225 among 29 713 cases—MacRae, 1948) The large majority of pregnant women with real heart disease have chronic rheumatic valvular defects, mostly mitral disease with more or less stenosis. Congenital defects, syphilitic aortitis, hypertension, subacute bacterial endocarditis, and thyrotoxicosis are relatively rare in pregnancy making up altogether less than 10 per cent of the cases of heart disease in pregnancy Of the 225 cases noted by MacRae (1948) 91.5 per cent were rheumatic, 5 8 per cent congenital, and 2.7 per cent of other types.

The important question concerning heart disease in pregnancy is the prognosis, one of the most difficult problems in medicine. Many patients, even with considerable mitral stenosis, go through pregnancy childbirth, and the puerperium without any difficulty whatever and with no obvious injury to the heart, although some authorities believe that even in such cases the strain eventually tells by shortening life. This is a supposition difficult to prove because of the fact that persons with mitral stenosis usually live short lives anyway and are prone to heart accidents or failure even though not subjected to the strain of pregnancy Some cases even without evidence of much heart disease do badly because of the development of atrial fibrillation, of recurrent rheumatic infection, or of unexpected heart failure during pregnancy No rule can be set, except that pregnancy should be forbidden or terminated early if symptoms and signs of heart failure appear early or if there have ever been such symptoms or signs the same advice applies when there are complications of atrial fibrillation, free aortic regurgitation, and hypertension. It is particularly these conditions—atrial fibrillation, heart failure, marked aortic regurgitation, and hypertension—that have been found by experienced observers to menace the lives of both mothers and infants. Functional tests are of little or no importance in prognosis in comparison to the structural lesions that are found (Hamilton, 1941) However even such conditions as marked mitral stenosis, coronary thrombosis, and heart block have not prevented normal pregnancy and delivery although it is certainly advisable to warn such patients against pregnancy except in the very rare case of uncomplicated congenital heart block. Although the presence of heart disease of any type or severity always adds to the risk of pregnancy the chance may often be taken, and even at moderate risk it may be justifiable to allow one pregnancy to occur and to continue if there is a great desire for a child. One must remember incidentally that all the strain is not from the pregnancy and childbirth the care of the child after birth and of the growing family may be the cause of greater strain.

Almost all the congenital cardiovascular defects have been represented among the successful cases except for those intensely cyanosed, septal defects, patent ductus arteriosus, and aortic coarctation have not been a bar Even subacute bacterial endocarditis with penicillin during pregnancy has been successfully treated with living mother and child, and uneventful pregnancies

have taken place in severely hypertensive women after successful reduction of their blood pressure by thoracolumbar sympathectomy

It is of the greatest importance to follow a cardiac patient through pregnancy with conscientious care and meticulous treatment. This care has already proved invaluable and is the chief therapeutic and preventive measure. In the nineteenth century the maternal mortality of pregnant cardiacs was almost 50 per cent (Zarday 1948) Hamilton (1941) has concluded that careful following of pregnant cardiac patients at the Boston Lying In Hospital has reduced the maternal mortality from about 12 per cent to less than 3 per cent in the past twenty years in his series of 1 000 pregnant cardiac patients, the first 500 showed a maternal mortality of 5 4 per cent and a fetal mortality of 18 0 per cent, while the second 500 did considerably better with a maternal mortality of 2 6 per cent and a fetal mortality of 15 8 per cent. The maternal death rate rose to 33 3 per cent in the presence of atrial fibrillation. MacRae (1948) reported a maternal mortality of 3 1 per cent, Lease (1948) one of 1.5 per cent, and Stromme and Kuder (1946) one of 1.3 per cent.

If termination of pregnancy is essential, the kind of anesthetic and type of operation (Cesarean section, or delivery from below) are less important than the skill, experience, and care of the anesthetist and operator Of a group of 74 cases of pregnancy with heart disease reported by Frey and Lardi (1928) all did well, 43 being allowed to go to term with spontaneous childbirth, 19 being operated on under local anesthesia by Cesarean section, and 12 cases being interrupted early in pregnancy This record is very unusual generally a mortality of about 2 per cent is reported in pregnant cardiac patients. One authority (Jensen, 1927) believed that the difference of opinion expressed in the literature concerning heart disease and pregnancy is due to the inconsistency of comparing massed statistics from public or large hospitals with figures from the private practice of experienced obstetricians. In general, it is much better to allow patients to go to term and to deliver themselves (with help, if necessary) than to interrupt pregnancy at an advanced stage. It is also best to avoid Cesarean section

For the immediate treatment of heart failure in pregnancy the usual methods, such as digitalis administration and diuretics, are indicated, but not termination of pregnancy at least until *after* the heart failure has been controlled for auricular fibrillation digitalis, quinidine or both should be employed. Apparently these drugs do not affect the fetus in a harmful way

Finally it is to be observed that the old tradition that the cardiac patient has a shorter or easier labor than the normal woman is not founded on fact (Nelson and Eades, 1935)

Anesthesia and surgical operations. Anesthetics and operative procedures do not cause heart disease, although serious poisoning of the heart may occur from the effect of chloroform, and abnormalities of the heart beat are common under anesthetics during operations. Chloroform and the newer related anesthetic cyclopropane may produce premature beats, paroxysmal tachycardia, and in experimental animals ventricular fibrillation and death, it is likely that

sudden death of patients during anesthesia by these agents comes in this same way; certainly they should be administered only by experts and never when the heart is already irritable or diseased. General anesthesia, with ether or ethylene and oxygen, and local anesthesia are the procedures of choice from the cardiovascular standpoint. During ordinary anesthesia premature beats, paroxysmal atrial tachycardia, and disturbance of the sinoatrial pacemaker have been noted by electrocardiographic study to be common, they are generally only of passing interest although alarm may be occasioned temporarily by the very rapid pulse of paroxysmal tachycardia which subsides as a rule without leaving any trouble behind it and sometimes is dramatically banished by carotid sinus pressure. Very rarely a paroxysm of tachycardia may be associated with a state of shock which proves fatal, in such cases it is the very low blood pressure and not the rapid heart action that is the serious sign. Anoxemia during anesthesia may produce temporary atrioventricular block. Spinal anesthesia is usually attended by a marked drop in blood pressure; in the presence of hypertension or serious coronary heart disease spinal anesthesia should be avoided or undertaken cautiously.

Patients with heart disease of nearly all types (rheumatic, hypertensive, coronary congenital, thyrotoxic) go through anesthesia and surgical operations surprisingly well, even with atrial fibrillation, heart block, or slight angina pectoris or congestive failure, provided care is used. But marked congestive failure, very recent coronary thrombosis (that is, within a few weeks) severe angina pectoris, marked aortic stenosis, and syphilitic aortitis add very appreciably to the operative risk, sudden death being a common ending for all of these conditions, operations of choice, for example, herniotomy interval appendectomy and often cholecystectomy and prostatectomy should be routinely avoided in such cases. If there is time, preoperative preparation of cardiac patients, when indicated, is usually helpful, such as saturation with digitalis for congestive failure or atrial fibrillation, except in rare cases, however the presence of heart disease should not deter one from emergency operations. In the presence of thyrotoxicosis congestive failure and atrial fibrillation may actually be cleared away by the operation itself (subtotal thyroidectomy) after suitable preparation with iodine (see Chapter 18) or by the newer use of irradiated iodine (see Chapters 21 and 30) It is also true that it is often wise to assume the risk of operation in cardiac patients for other conditions which are proving intolerable for life or comfort, for example, lumbodorsal splanchnic resection for severe hypertension in youth or middle age (see Chapter 19) and resection of the prostate gland for urinary obstruction (Mallory et al., 1943)

In thoracic surgery routinely and when disturbing arrhythmias are present or threaten in other surgical fields protection of the patient by the administration of quinidine sulfate orally or parenterally (e.g., 0.2 to 0.4 gm, 3 to 6 gr every 2 to 4 hours during the necessary period of time) may prove very helpful or even lifesaving.

Collapse or death during anesthesia or surgical operation is rarely due to heart trouble; it is almost invariably the result of shock from hemorrhage,

infection, trauma, or other cause and the treatment of such collapse should not be directed at the heart but at the condition of shock, hemorrhage, or infection. For cardiac standstill, however the heart should be massaged with the hand through the incised diaphragm if the abdomen is open, or the thorax itself can be opened in the emergency if not already entered in the course of thoracic surgery Moreover if the heart is normal to start with, epinephrine (adrenaline) chloride (solution of 1 to 1 000) may be injected within two or three minutes directly into the heart (0 25 to 0.5 cc) to restore a normal beat in some cases. There have also been introduced devices to stimulate the heart to resume its beating or to abolish ventricular fibrillation by the use of electric shocks (Hyman, 1935 Beck, 1941 and 1947)

Sufficient authentic recoveries by these procedures have by now (1951) been reported to make them advisable in every case of cardiac standstill during anesthesia, the first method, namely that of massage, is far preferable to the second since epinephrine may itself, especially when applied directly to a diseased or irritable heart, induce ventricular fibrillation and death. The value of the massage combined with artificial respiration was demonstrated some years ago in a spectacular case of recovery at the Lahey Clinic 20 minutes after the heart had ceased its spontaneous beating (Adams and Hand, 1942)

Postoperative complications may include so-called "heart attacks" or cardiac emergencies, in particular paroxysmal tachycardia and paroxysmal atrial fibrillation, and coronary thrombosis angina pectoris and acute pulmonary edema (with or without asthma) or other evidences of congestive heart failure are not common, even in the presence of serious heart disease, largely because the patients are having a regime of complete rest. It is important when the cardiac reserve is low to avoid much saline solution by vein before or after operation since the extra sodium may precipitate pulmonary or systemic congestion with edema. Procaine in 0 1 per cent solution intravenously has been helpful in dispelling bothersome ectopic tachycardia during surgical operations. Disagreeable abdominal complications, such as excessive intestinal gas, may however precipitate heart trouble in those likely to have it. More common postoperatively than serious cardiac conditions is the frequent complication of *pulmonary embolism* which may itself give rise to the acute cor pulmonale and be confused with coronary thrombosis or acute pulmonary edema of cardiac origin (see Chapter 20) It demands search for venous thrombosis in the legs and ligation of the thrombosed veins bilaterally since both legs are usually involved—this may be a lifesaving measure (see Chapter 28)

Excessive ingestion of food and fluid and salt. *Overeating* may have, so far as the heart is concerned, a few untoward sequelae. In the first place, a state of obesity ill health, and fatty infiltration of the heart may result from the excessive ingestion of food, and, secondly heart failure, atrial fibrillation, angina pectoris, or acute coronary thrombosis may be precipitated by a hearty meal, especially if followed at once by vigorous exertion or by horizontal recumbency This association between hearty eating and coronary thrombosis

or angina pectoris occasioned the one-time erroneous diagnosis of rapidly fatal acute indigestion."

Ingestion of excessive fluids and salt (sodium). It was long thought that the ingestion of excessive amounts of fluid daily for long periods of time might lead to cardiac enlargement and failure, and the most typical example of such a state was called the "beer heart." It was reasonable to believe that the increased work required of the heart to dispose of the enormously increased amount of fluid absorbed into the circulation by the copious beer drinking of former times (sometimes as much as 30 liters of beer a day were ingested routinely by champions" in Munich) might lead to cardiac hypertrophy and dilatation (Bollinger 1884) however doubt was later cast on this idea by the fact that hypertension undoubtedly existed in many individuals but was unsuspected in the days before blood pressure measurements. Occasionally large hearts are still found with no other explanation than that they are "beer hearts." However evidence against the existence of the "beer heart" is the finding that ingestion of very large amounts of water (comparable to the volume of beer drunk by the "champions" of former days) by patients with diabetes insipidus does not apparently cause cardiac enlargement (Rowntree, personal communication, 1930)

The immediate effect of excessive fluid and salt (sodium) ingestion or injection is sometimes clearly seen as an injurious one in the case of a weakened heart or circulation. It is known that temporarily the blood volume may be much increased by the ingestion of an excessive amount of fluid containing salt, especially if the kidneys are slow to function. In recent years when the forcing of fluids has been a common therapeutic procedure in the treatment of acute infection, and especially in the stimulation of kidney secretion and the washing out of kidneys and bladder in cases of prostatic hypertrophy before and after operation, the strain on the heart and circulation of weakened patients has sometimes manifested itself by the development of dependent edema, or by the precipitation of acute pulmonary edema (with or without cardiac asthma) or angina pectoris. The intravenous injection of considerable amounts of normal saline solution (500 to 1 000 cc for example) has also on occasion been the cause of accidents because of the strain on the heart. While the forcing of fluids continues, rest, digitalis, and other such measures may prove ineffective. It is usually a simple matter to establish a compromise between the surgeon and the physician in the matter of the amount of salt and fluid intake in a surgical patient subject to angina pectoris or congestive heart failure. Glucose solutions may helpfully replace saline on occasion. And in a cardiac patient acutely or chronically ill with congestive heart failure the one final measure that may lead to recovery temporary at least, after other measures have failed, is salt (sodium) restriction. (See Chapter 30 and Bibliography at end of this chapter)

Gastrointestinal diseases and disorders. *Indigestion,* aside from overeating which I have just discussed, is related to heart disease in three ways (1) as an associated, not a causative, factor (2) as an irritating or aggravating factor

in the production of disorders of heart function whether the heart is normal or diseased and (3) as a cause of confusion in diagnosis. Thus, it is common for *spasm of esophagus or stomach (cardiospasm or pylorospasm) hiatus (diaphragmatic) hernia of the stomach, gallbladder disease (with or without stones) irritable or sluggish colon (with constipation) and much "gas" in stomach and intestines* (often consisting of swallowed air—"cribbing") to be present in a person who has heart disease, particularly of the hypertensive or coronary type. This association is mainly an incidental one, dependent primarily on two factors, both common denominators, namely (1) the aging process and (2) a type of individual or manner of life. That a closer association does not exist is shown, for example, in the case of gallstones and coronary atherosclerosis of high degree, which occur together twice as commonly as separately by the following facts (1) the former gallbladder disease, is more common in women while the latter coronary heart disease, is more common in men, and (2) the youngest cases of either condition are uncomplicated (Walsh, et al. 1941) Peptic ulcer is no more often found with heart disease than without it.

The second connection between these various gastrointestinal disorders and heart trouble, namely that of provocation of symptoms, is an important practical problem and often demands careful study and skillful treatment. Extrasystoles, paroxysmal tachycardia, and even atrial fibrillation, can be excited reflexly by gastrointestinal disorders even in a normal heart, subsiding when the indigestion ceases. Sometimes serious disorders of function, angina pectoris and congestive failure, can be prevented or relieved in a cardiac patient by straightening out the digestive trouble, and from the standpoint of the sufferer from indigestion gastrointestinal symptoms may be relieved by correction of disorders of the circulation. However radical measures of treatment, such as cholecystectomy are not to be undertaken lightly hoping to get rid thereby of some such condition as angina pectoris. Emergency operations may be justified, but a cardiac patient may be made worse, with the precipitation even of myocardial infarction or death, by an operation of choice or convenience.

Cirrhosis of the liver due to heart disease is uncommon. Only 35 cases were found by Garvin (1943) among 790 consecutive adult autopsied patients who died of heart disease, most commonly in those who had had chronic or recurrent congestive failure secondary to rheumatic heart disease (14 of 119 cases) or to hypertensive heart disease (14 of 264 cases) In my experience the more definite cases have been those with congestion due to mitral stenosis, with or without tricuspid stenosis, and chronic constrictive pericarditis, but it is important to note that the liver may be engorged with blood and ascites may be present in such cases for a long time before any appreciable cirrhosis of the liver develops.

Finally perhaps the most important relationship between heart trouble and indigestion is that of confusion in diagnosis often their symptoms re-

semble each other closely particularly angina pectoris and the pain of cardiospasm on the one hand and the acute symptoms of myocardial infarction and gallstone colic on the other (see Chapter 21) the skill of the physician to distinguish them may be taxed to the utmost, particularly when, as so often happens, both conditions cause symptoms in the same person and at the same time.

Renal disease and uremia. *Acute hemorrhagic nephritis* particularly in children, may be accompanied by severe myocardial involvement with cardiac dilatation and even failure, which tend to subside as the nephritis clears (Ellis, 1936 Master et al., 1937 Langendorf and Pick, 1938 Rubin and Rapoport, 1938 Whitehill, Longcope, and Williams, 1939) this is not hypertensive heart disease.

Chronic nephritis has no direct bearing on the heart until renal insufficiency with *uremia* and potassium poisoning develop (see section on Poisoning) Nephrosis with edema and salt-losing nephritis are important conditions which may complicate or indeed simulate cardiovascular disease and, of course, chronic nephritis frequently complicates though it rarely initiates hypertensive disease.

Collagen diseases and allergy There is an interesting and puzzling group of closely related diseases which involve the collagenous (connective) tissue of the body primarily often including that of the heart, and which may be due to an allergic type of reaction. One of these conditions is *disseminated lupus erythematosus* ("diffuse collagen disease) which has attracted much attention of late in this disease of unknown cause polyserositis with pericarditis is common and there may be also endocarditis and myocardial involvement and even congestive failure. *Polyarteritis (periarteritis) nodosa* is another rare but important disease of unknown origin, sometimes attended by a high count of eosinophiles in the blood, which also involves the viscera, including the myocardium, by causing a nodular reaction in the walls of the small arteries often leading to occlusion and local necroses (see Chapter 28) In the *Libman-Sacks syndrome* attended, like the other two diseases mentioned above, by skin manifestations in some of the cases, there has been described an atypical verrucous endocarditis. In some cases of *scleroderma*, myocardial changes, leading to fibrosis and failure, have been found. In *rheumatoid arthritis* also of unknown etiology pericarditis and endocarditis and myocarditis (even with partial heart block as shown by a long *P R* interval) may occasionally appear as complications not to be ascribed, at least in most cases, to a coincident rheumatic fever In a series of 45 autopsied cases of rheumatoid arthritis studied at the Massachusetts General Hospital 45 per cent showed involvement of the pericardium, 17 per cent of the myocardium, 20 per cent of the endocardium, and 10 per cent of the aorta, probably the result of the etiologic factor behind rheumatoid arthritis itself. In several cases there were nodules in the pericardium and other tissues almost pathognomonic of the disease.

Also a *serum carditis* and deleterious effects of *anaphylaxis* (allergy) on the myocardium have been described. Electrocardiographic abnormalities are common in these various diseases. How much all these different conditions (even including rheumatic fever) are related in etiology and especially in their effects on the heart and blood vessels we do not yet know but there does seem to be some sort of definite relationship, which is further borne out by the favorable effect on nearly all these conditions, at least pro tem, by the new hormonal therapy with adrenocorticotropic hormone (ACTH) and cortisone.

Miscellaneous conditions. Before this part of the book is concluded there are various other cardiovascular relationships which, though rare, unimportant, or poorly understood, deserve mention. Some of these were included in the long list of miscellaneous causes of minor abnormalities of the heart culled by von Bonsdorff from the records of the Boston City Hospital some years ago (1939) but there are still others of possible interest.

Associated with acute hypertension in the *toxemias of pregnancy* (eclampsia) there may be serious toxic myocardial dilatation with acute heart failure and pulmonary edema. The heart may dilate also in the severe stages of the toxic reaction to *burns* and *exfoliative dermatitis*.

Polyserositis of high degree and long course and of unknown etiology is associated with a good many of the cases of chronic constrictive pericarditis; a few of such cases are clearly due to tuberculosis but probably most of them are of that origin (see Chapter 27).

Amyloid, sarcoid, xanthomatous and *hemochromatous* myocardial lesions are uncommon but striking in their pathologic pictures. They are of obscure origin, difficult to diagnose, and as a rule but a part of widespread systemic diseases. *Amyloid disease* consists of the infiltration of various organs and tissues in the body, especially spleen, liver and kidney, with amyloid, a glycoprotein, the product as a rule of a long-continued wasting disease such as tuberculosis, septic suppuration, syphilis, chronic arthritis, anemia, and cancer; the heart is not usually seriously affected but very rarely there may be so-called primary amyloid disease of the coronaries, myocardium, and blood vessels with death from myocardial failure (Binford, 1940). *Sarcoid disease* or Boeck's sarcoidosis, consists of a benign lymphogranulomatosis, with hard tubercles, composed of epithelioid cells surrounded by lymphocytes without caseation, which involve various organs in the body but especially lymphoid tissue; the etiology is unknown and the disease has often progressed extensively before it is discovered, for it is usually symptomless at first; the mediastinal glands and lungs and spleen are particularly the site of the lesions; the myocardium and epicardium are sometimes involved, but not as a rule to any important degree; no cure is known but recovery is not uncommon. *Xanthomatosis* consists of the infiltration of various tissues and organs of the body, including the skin and the heart itself, with nodules or masses of cholesterol and cholesterol esters. It is a complication of a disturbed metabolism of cholesterol fats, often hereditary, and is sometimes seen in diabetes

mellitus its chief importance so far as the heart is concerned is its association with serious and early coronary arterial atheromatosis which may lead to angina pectoris, coronary occlusion with myocardial infarction, and cardiac death. *Hemochromatosis* may seriously involve the myocardium with deposition of iron in the muscle fibers and with resulting cardiac enlargement and failure, and it may cause marked atrophy and pigmentation of the adrenal glands (Graef, et al. 1949)

Finally certain central and peripheral nervous diseases and abnormalities of skeletal musculature in function or in structure, such as myasthenia gravis and progressive muscular dystrophy may be attended by heart muscle disease, usually of mild degree, while there remain a few mysterious cardiac diseases, such as *Fiedler's acute isolated myocarditis* (see Chapter 25) and Davies endomyocardial necrosis and fibrosis (see Chapter 25)

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PART III

STRUCTURAL CARDIOVASCULAR ABNORMALITIES

CHAPTER 24

IMPORTANCE, DIAGNOSIS AND INCIDENCE OF STRUCTURAL CARDIOVASCULAR ABNORMALITIES

In order to keep this volume within reasonable bounds in size which the addition of accounts of important new advances has already threatened to exceed, it has proved possible to condense considerably certain portions of Part III, in particular the chapters on Myocardial Disease and on Vascular Disease. The reader is referred for further details to the sections on Pathology in the chapters of Part II of this book and to publications on pathology and on the peripheral circulation per se

The consideration of structural alterations in the heart and great vessels naturally follows a discussion of the fundamental causes that are responsible for them. Although this pathologic field is important, it is often neglected. A generation and more ago it was the chief subject for discussion in heart disease and was much too predominant, but then a vigorous reaction took place and the pendulum swung too far the other way: interest became overwhelmingly centered on physiologic aspects of the circulation with a disregard of actual cardiovascular lesions. A return to a study of structural pathology has been a healthy sign.

Structural abnormalities of the heart affect, often to a very important degree, the mechanics and the functional state of the circulation. Not only may high blood pressure, infection, endocrine deficiency anemia, and blood chemical influences seriously affect the heart with little to be found structurally wrong with it, unless the conditions are chronic, but pathologic lesions alone in their turn, too may cause serious cardiovascular strain, as in the case of mitral stenosis, aortic regurgitation, myocardial infarcts, and congenital defects. We may find the cause of heart failure and death in one of these organic lesions just as we may find it in some condition entirely outside of the heart and great vessels. It behooves us therefore to look for structural abnormalities in every cardiac patient as well as for evidence as to etiologic factors and as to the functional state of the circulation. Such search is now routinely carried out by

the usual methods of examination which include inspection, palpation, auscultation roentgenology and electrocardiography and now cardiac catheterization is also becoming routinely available to aid especially in the diagnosis of certain abnormalities, congenital and acquired, by x ray visualization of the catheter and by determination of the blood oxygen content and pressure in the superior vena cava, right atrium right ventricle and pulmonary artery (see Chapters 10 and 13 in particular)

Much has appeared in the medical literature about mistakes in diagnosis, including the diagnosis of heart disease, and there have been various efforts to correlate antemortem and postmortem diagnoses. It has been shown that more careful history taking and physical examination including more correct appraisal of auscultatory findings, as well as the use of other methods of study like electrocardiography and roentgenology have in recent years reduced greatly the errors of cardiovascular diagnosis, but there are likely to remain some pathologic conditions that cannot be diagnosed clinically In other words not only may errors arise from carelessness or incomplete study but errors may also be due to the very fact that some structural abnormalities give rise to no clinical symptoms or signs, and so even under the most favorable circumstances are undiagnosable. Such abnormalities include (1) acute or lesser grades of chronic endocarditis involving valves or heart chambers with little or no valvular deformity (2) lesser grades or earlier stages of coronary atherosclerosis and narrowing, (3) slight aortic disease, whether aortitis or atheromatous, (4) relatively slight myocardial involvement consisting of hypertrophy of muscle fibers or of degenerative or inflammatory changes, and (5) acute or chronic pericarditis of lesser degrees without friction rub or definite signs of effusion, enlargement, compression, or fixation of the heart. Moreover sometimes the very first attack of coronary insufficiency or the onset of acute coronary thrombosis may be rapidly fatal.

Errors of diagnosis may thus be divided into three groups first, those that are preventable because they are due to well-marked lesions and should be discovered if careful and complete examinations are made second, those that may or may not be preventable because the lesions are slight to moderate in degree and sometimes give signs and sometimes do not; and, third, those that are so slight or cause so little strain that no signs ever result. Most of the diagnostic errors in cardiovascular disease when careful clinical work is done fall into this last category and the clinician need feel no chagrin when the pathologist discovers some slight lesion that could be of no clinical importance or could give rise to no symptoms or signs.

Since the clinical diagnosis of organic heart and aortic disease is based on the finding of enlargement, valvular lesions, pericarditis, aortic dilatation, and congenital defects (except in a few cases without these findings but with angina pectoris or important abnormalities in cardiac function revealed by electrocardiography) it may be said that about 2 per cent of the population of much of the world show during life signs of organic heart disease through the presence of structural cardiovascular abnormalities, varying very much with age, from less than 1 per cent in childhood to 10 per cent or even much

more in old age, increasing with each added decade. Many of such abnormalities are of little importance, often of far less importance than symptoms like angina pectoris in cases that happen to show no signs of structural defects. At postmortem examination the pathologist finds that far more than 1.5 to 2 per cent of hearts or great vessels show abnormalities. Most of these abnormalities are, however small and unimportant and do not constitute real disease, or else they are terminal and not diagnosable clinically Nearly half of all cases examined post mortem at the Massachusetts General Hospital from 1896 to 1919 showed cardiovascular lesions (1,906 out of 4 000 autopsies) but these were often trifling (Cabot, 1926)

Of patients actually seeking advice because of cardiac symptoms or signs, the percentage of those with organic lesions, that is, structural abnormalities, varies considerably in different groups, for example from 22 per cent in a small group of cases noted in private practice (Cabot, 1926) to 62 per cent in a larger group (1 000 cases) seen in consultation (White and Jones, 1928) and 87 per cent in a group of 1 000 general hospital cases (White and Jones, 1928) Since many individuals with symptoms or signs of cardiac nature never visit the hospitals but nevertheless are sufficiently bothered to consult their own private doctors, the last figure is much too high to represent the average. Cabot's series is too small to have any but suggestive value, although it is quite likely that it is near the correct figure for the community at large, including all individuals with cardiac symptoms or signs who do not bother to obtain medical advice. Of the total of those cases who because of cardiac symptoms or signs do visit doctor or hospital the intermediate figure of 50 per cent probably represents reasonably well the number who have organic heart disease

Of the various abnormalities enlargement of the heart is by far the most common, with valvular disease next, and aortic disease pericarditis, and congenital defects less frequent. Of a series of 1,846 cases with cardiovascular lesions found at postmortem examination at the Massachusetts General Hospital Cabot reported that 1,209 (65.5 per cent) "were recognized by the pathologist as having some enlargement of the heart (Cabot, 1926) In many of those who showed no enlargement in this series the lesions were too trivial to be dignified by the term disease. Myocardial infarcts were recorded in only 26 cases (1 3 per cent) acute in 20. Valvular defects (but not necessarily deformity sufficient to cause either regurgitation or stenosis) were present in 21 per cent of 1,230 autopsied cases of Cabot's cardiac series, including "latent" as well as manifest lesions. Pericarditis was present as an acute, often terminal, condition in 9 8 per cent of 1 906 cases of his series, and as a chronic, often silent, condition in 6 per cent more, while syphilitic aortitis was found in 5 per cent, aneurysms in 2 per cent, and congenital defects in 1.5 per cent. In comparison among the last 100 cases with significant cardiovascular lesions autopsied at the Massachusetts General Hospital (September 1949) there were 70 cases with cardiac enlargement, 47 cases of myocardial infarction (16 acute 31 chronic) 6 cases of valvular defects (7 mitral alone 4 aortic alone, 15 both, 0 tricuspid) 5 cases of acute pericarditis, 7

cases of chronic pericarditis, 3 cases of syphilitic aortitis, 0 cases of aortic aneurysms (dissecting in 0) and 3 cases of congenital defects.

Of a series of 1 000 clinical cases of organic heart disease in northeastern United States, Dublin reported (1925) that 88 per cent showed cardiac enlargement, 44 per cent mitral stenosis, 15 per cent aortic insufficiency 3 per cent aortic stenosis, 17 per cent aortitis, and 1+ per cent aneurysms. Of another clinical series of 2,314 cases of organic heart disease in New England, 47 per cent showed valvular disease, 4 per cent syphilitic aortitis, 3 per cent pericarditis, 2 per cent congenital defects, 0.5 per cent aneurysms, and the large majority showed definite cardiac enlargement (White and Jones, 1928) this series included many private patients living in an enlightened community and had much less syphilis than the other groups cited, a state of affairs still more evident now with the passage of time—at present far fewer than 1 per cent of my own private patients have syphilis, even as a latent condition.

The pathologic lesions found in cases of sudden death are also of especial interest. In one series of 198 individuals (Bedford, 1933) organic heart disease was found in 122 (62 per cent) of whom 81 per cent were males and 19 per cent females. Nonvalvular disease (87 cases) was over twice as common as valvular disease (35 cases) Atherosclerosis of the coronary arteries of an important degree was present in 63 cases (57 males and 6 females) In 33 patients there was gross myocardial fibrosis, with definite infarction in 27 and in 6 rupture of the heart wall had occurred at the apex of the left ventricle. Gross fatty infiltration of the heart was found in 2 females. The aortic valve alone was diseased in 20 cases, the mitral valve alone in 7 and both in 8. An aneurysm of the aorta was found in 22 cases, of the dissecting variety in 2. Syphilitic aortitis involving the coronary artery mouths occurred in 13 cases.

In another series of 130 cases of sudden death (Munck, 1931) 74 (57 per cent) showed well-marked coronary artery disease, and 33 (25 per cent) had syphilitic aortitis.

In two of the largest series of autopsied cases of sudden death there were the following findings (1) 2,000 in number (Martland, 1940) organic heart or aortic disease was found in 1,590 (79.5 per cent) 1 115 of which were of coronary or hypertensive type, 262 syphilitic, 116 rheumatic, while 731 showed extensive coronary artery disease, of which 304 had acute thrombosis and (2) 2,030 in number (Helpern and Rabson, 1945) cardiovascular disease in 59 per cent, of which more than half were "coronary" cases (see Chapter 34 for further details)

Of some special interest is a recent analysis of the postmortem findings at the Massachusetts General Hospital and Boston City Hospital (Medalia and White, 1951) of individuals dying at the age of 50 years or more. This gives some idea of the expected findings in older people. The following were the incidences of the "underlying and contributing causes of death" in both males and females (Table 11)

A report has just been published from the Geriatric Clinic of the Peter Bent Brigham Hospital in Boston entitled *Diseases in Old Age A Clinical and Pathological Study of 7,941 Individuals Over 61 Years of Age* (Monroe

Table 11

THE PREVALENCE OF UNDERLYING AND CONTRIBUTING CAUSES OF DEATH AFTER THE AGE OF 50 IN 1,251 INDIVIDUALS AT THE MASSACHUSETTS GENERAL AND BOSTON CITY HOSPITALS

	6th Decade	*7th Decade*	*8th Decade*	*9th Decade*
Totals	313	340	286	312
Coronary sclerosis	144	224	222	262
Atherosclerosis, including coronary sclerosis	215	243	251	305
Nephrosclerosis	71	107	111	171
Cerebrovascular lesions	32	31	43	68
Bronchopneumonia	81	116	105	147
Liver and gallbladder disease	44	84	68	81
Cancer	68	83	85	67
Tuberculosis	39	30	34	14
Gastric and duodenal ulcers	25	20	26	21

1951) "Clinically only 44 6 per cent of the patients in this series had no heart disease but the pathologists found a much smaller fraction than that, for only 28 5 per cent of the men and 28.3 per cent of the women had normal hearts out of 1 177 autopsies." The heart weights at autopsy were compared. In the normal men, 61 to 85 years old, the heart weights ranged from 302 to 373 gm while in the normal women of the same age the weights ranged from 274 to 304 gm. In the cases of valvular heart disease the average weight of the heart in old men was 549 gm and in old women 439 gm. Finally the heart weight in cases of nonvalvular disease averaged 526 gm in old men and 426 gm in old women when there was coronary artery occlusion and 493 gm in the old men and 394 gm in the women without coronary artery occlusion.

In all this discussion of structural changes in the heart and great vessels it is of the utmost importance to recognize the wide range of the normal, a range which has not yet been adequately determined and the very wideness of which makes it difficult or impossible to identify slight abnormalities. For a full discussion of the range of the normal heart the reader is referred to Chapter 2 and for certain normal measurements to Table 12 which appears at the end of this chapter One particular measurement, as an example, may be appropriately referred to here: namely that of heart weight.

The normal heart weight bears a fairly definite relation to body weight, 0 40 to 0 45 per cent, but ranging from 0.35 to 0.50 per cent, lower values being found more often in women and obese individuals and higher values in men and thin persons. The normal heart weight may be calculated from the body weight with an error up to about 10 per cent. The weight of the heart in the normal adult male averages about 300 gm and in the female about 250 gm. The limits of the normal range of weight of the adult heart are 200 and 350 gm. Heart weight has been related also to body length (Zeek, 1942) Heart volume and certain other measurements are to be found in Table 12.

Table 12

NORMAL ANATOMIC CARDIAC MEASUREMENTS

Weight (gm)	
Adult	
Range	200–350
Average male	300
Average female	250
Percentage of body weight (Smith)	
male	0.43%
female	0.40%
Child (Vierordt, Muller)	
Birth	20–25
1 month	15–20
6 months	20–25
1 year	30–40
2 years	45–55
4 years	65–75
8 years	95–105
12–16 years	150–250
Left ventricle: right ventricle	
Birth 1:1	
Adult	
Range 1.7:1 to 1.95:1	
Average 1.85:1	
Individual chambers (adult)	
Left ventricle	130
Right ventricle	70
Left atrium	24
Right atrium	25

Volume and Capacity (cc)	
Heart tissue (Benecke)	
Birth to 3 months	20–25
1 year	30–35
6 years	65–75
10 years	110
15 years	130–175
Adult	210–290
Capacity of chambers in adult (average) (Hochrein)	
Right atrium	163
Right ventricle	137
Left atrium	140
Left ventricle	121
Total (4 chambers)	561

Thus the *total volume of the filled heart* averages 811 cc (561 + 250) from these figures; *during life* the heart volume is never so great since all four chambers are not full at the same time—this would mean a subtraction of about 200 cc from the volume stated above leaving approximately 600 cc

Other Measurements (adult)	
Ventricular wall thickness (midway between base and apex and not including papillary muscles)	
Left	10–12 mm
Right	3–4 mm
Ventricular septum	9–12 mm
Valve circumferences (cm)	
Tricuspid (Average 12)	11–13
Mitral (Average 10)	9–11
Pulmonary	8–9
Aortic	7–8
Valve areas (sq mm) (Creutzfeldt)	
Tricuspid	2,380
Mitral	1,590
(Dexter et al.)—During life	
Mitral	4,000–6,000
Heart length (longitudinal diameter in cm) (Average 11 cm)	10–12
Heart width (transverse diameter in cm) (Average 9 cm)	8–10
Heart depth (anteroposterior diameter in cm) (Average 7 cm)	6–8

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CHAPTER 25

MYOCARDIAL DISEASE
CARDIAC ENLARGEMENT HYPERTROPHY AND DILATATION
MYOCARDITIS

The myocardium is the most important part of the heart. If it is sound, great deal of disease of endocardium and pericardium and great vessels, valvular deformities and septal defects, and of strain from hypertension can endured for a surprising number of years. If it is seriously diseased or fai death may come quickly even though all the rest of the cardiovascular syste is perfect.

Myocardial disease includes various abnormalities. The most common a hypertrophy and dilatation (due fundamentally to the strain of greatly i creased work) and the degeneration and fibrosis due to coronary insufficienc Less frequent are inflammatory changes, or true myocarditis, atrophy fro and malnutritional changes, fatty degeneration from severe anemia, fat infiltration, congenital defects, neoplasms, and traumatic lesions.

Dilatation of the heart chambers is a very common condition, occurri sometimes as a compensatory reaction to valvular disease and sometimes as natural sequence of a failing heart muscle under the effect of the conditio *which cause myocardial disease itself*.

Enlargement of the heart, which includes both hypertrophy of muscle an dilatation of chambers, will be considered first since it is by far the mo common of all cardiac abnormalities.

CARDIAC ENLARGEMENT HYPERTROPHY AND DILATATION

Cardiac enlargement is the commonest and most important evidence o heart disease. Often it can be taken as an index of the degree of cardiac stra since a very large heart indicates a great cardiovascular burden and an un favorable prognosis while a small heart indicates a small degree of cardia strain and a favorable prognosis except in the presence of serious coronary

disease. It is to be noted at the outset that very important heart or aortic disease may be present with little or no enlargement, examples of this are occasional cases of syphilitic aortitis, of angina pectoris, and of coronary narrowing leading shortly to thrombosis with cardiac infarction. Usually however a diseased heart is enlarged, and its increase in size can be made out in many cases by clinical study alone, although roentgenologic control is often invaluable.

Enlargement of the heart may be due to hypertrophy dilatation, or both. The combination in varying degrees is much commoner than either condition alone except for very slight hypertrophy discoverable only at autopsy It is the dilatation rather than the hypertrophy that accounts for most of the increase in volume, especially of the largest hearts. In fact hypertrophy alone or with little dilatation may increase the heart size extraordinarily little and in early stages is not discoverable clinically as in the case of many patients with hypertension. A preponderant muscle weight increase gives rise to the so-called concentric hypertrophy of the heart. When in the course of time the heart begins to fail and grossly to dilate, or when there is a constant demand for an increased output as in aortic regurgitation, the hypertrophy is associated with dilatation and is then called eccentric. Another factor influencing the so-called concentric and eccentric types of hypertrophy is the state of the heart muscle at the time of death and at the postmortem examination If the heart stops in systole (contracted) the appearance of concentric hypertrophy is increased, if in diastole (dilated) the appearance of eccentric hypertrophy is increased.

Enlargement of the heart up to a weight of 425 gm may exist in a big man without clinical signs but hypertrophy of the heart beyond that weight should be found by clinical study Dilatation occurs as an important secondary factor if dilatation is absent, slight cardiac hypertrophy may exist with no clinical evidence thereof except on occasion when studies are carried out serially by x-ray or precordial electrocardiography if dilatation is present, the heart may be obviously enlarged clinically with little or no hypertrophy as in some cases of acute dilatation following acute coronary thrombosis with myocardial infarction.

The cause of cardiac enlargement is heart strain, whether intrinsic, that is, due to valvular disease, myocardial infarction, or true myocarditis (as in acute rheumatic fever) or extrinsic, due to hypertension, chronic thyrotoxicosis, or severe anemia. The strain may be acute or chronic overwhelming or slight. The speed of enlargement of the heart and the preponderance of hypertrophy or of dilatation appear to depend in part on these factors of time and degree. A quick occlusion of a large coronary artery may result in rapid cardiac enlargement due to dilatation, with the development of hypertrophy on recovery On the other hand, hyperpiesia (essential hypertension) slowly beginning, causes only gradual enlargement, hardly to be made out on clinical examination and consisting primarily of hypertrophy the dilatation appearing later when the heart begins to fail and to enlarge more rapidly Mitral stenosis simi-

larly acts slowly on the heart size, involving the right ventricle instead of the left.

The most common factors of heart strain giving rise to enlargement of the heart are hypertension of the essential type, valvular disease, of rheumatic or syphilitic origin, and myocardial infarction. Even in New England where rheumatic heart disease is the commonest of all clinical types producing cardiac symptoms and signs, cardiac enlargement is more often found at postmortem examination without, than with, valvular disease.

Less common causes of cardiac enlargement than hypertension and valvular disease are true myocarditis (especially during a severe rheumatic infection in childhood) cardiac infarction from severe coronary disease, thyrotoxicosis, chronic pulmonary disease (extensive fibrosis, as in silicosis) and congenital defects. Rare causes are arteriovenous aneurysms, severe anemia, beriberi, hypothyroidism (myxedema) thoracic and spinal deformities, chronic pericarditis with external adhesions, and cardiac neoplasms. Finally cardiac enlargement is occasionally of unknown cause undoubtedly there exist causes of enlargement still unrecognized or poorly understood. A few possible factors not yet clearly recognized as causes of cardiac enlargement are as follows. A severe infection rheumatic or otherwise, may cause so much myocardial damage that the heart dilates and does not recover sufficiently to return to its normal size, whether the valves are damaged or not, excessively severe or prolonged physical strain, as in athletic sports, may rarely in the case of a sensitive heart produce some permanent cardiac enlargement prolonged and excessive tachycardia in certain arrhythmias (especially atrial flutter and fibrillation) may be to blame in a minority of patients so afflicted, but particularly in infants a rare case of congenital idiopathic cardiac hypertrophy of lesser degree may survive to adolescence or adult life a combination of two or more of these factors is the most probable of all. Therefore it is unwise as yet to label every large heart of unknown type "hypertensive without more proof.

Hypertrophy Hypertrophy consists of the increase in size of the individual muscle fibers and apparently not in their increase in number at least in adults, although MacMahon (1937) has reported finding in infants and children a true active proliferation of the heart (with mitotic nuclear division) and regeneration of the myocardium following severe injury A comparative study has been reported of the size of muscle fibers seen in a normal heart weighing 300 gm, in a hypertrophied heart weighing 500 gm, and in an atrophied heart weighing 165 gm. The ratio of muscle fiber size was 5 9 4 respectively (Karsner Saphir and Todd, 1925) An important feature of myocardial hypertrophy after maturity is the apparent failure of the blood supply to parallel in its growth that of the muscle fibers· the ratio of one capillary to one muscle fiber in the adult remains throughout life no matter how large the heart becomes, resulting in a relative coronary insufficiency in an enlarged heart compared to the normal (Roberts and Wearn, 1941)

Whether the increased work and strain alone are primarily responsible or whether the hypertrophy is the reaction to trauma of the muscle fibers and primary dilatation due to the strain, as has been suggested, we do not know but we are aware of the fact that increase of the bulk and weight of the myocardium commonly follows considerably increased work if long sustained, and that it occurs in the part of the heart primarily involved. Although the heart is made up of complex masses of muscle continuous between the ventricles and between the atria respectively hypertrophy and enlargement may be very limited in location, as in the case of left ventricular hypertrophy in hyperpiesia and of right ventricular hypertrophy in pulmonary valve stenosis. When other factors like congestive failure appear the enlargement spreads to involve other parts of the heart for example, a failing hypertensive heart with functional mitral regurgitation shows, secondarily enlargement of left atrium and of right ventricle Although it is common in the end stages of heart disease and failure or in combined strains to find general enlargement of the whole heart, it is important to recognize that at first the enlargement may be entirely limited to one heart chamber sometimes with slight atrophy of another and that such limited enlargement may persist for years or that it may always preponderate. A discussion of the factors responsible for enlargement of the individual heart chambers will begin on page 650 All of the muscle of the heart wall of any given chamber whether atrial or ventricular (and including the papillary muscles) apparently takes part in the hypertrophy Finally it is important to realize that a structurally sound hypertrophied heart muscle may dilate and fail, even though the muscle cells show no degeneration post mortem.

In 1910 Bernheim introduced the concept of right ventricular obstruction and failure secondary to marked bulging of the septum into its cavity in cases of gross hypertrophy of the left ventricle. However the adaptability of the eccentric right ventricle to such a heart shape and the rarity of convincing proof have caused a debate as to the existence of such an entity (Evans and White, 1948 Russek and Zohman, 1950· Wilson and Zimmerman, 1950)

Dilatation. Dilatation of the heart is a very common condition, frequently occurring along with hypertrophy as a part of cardiac enlargement. It consists of a stretching of the heart wall due to a weakening or atonic state of the muscle or to a response to the physiologic demand for an increased output of blood per beat (as in exercise or in compensation for valvular regurgitation or anemia) If the cause of such acute dilatation ceases, the heart regains its usual size unless the injury has been irreparable. Often the dilatation persists or increases with continuance of the strain the tone of the muscle may partly recover but a permanent stretching of the fibers may persist. In some instances enlargement of the heart due preponderantly to dilatation may decrease clearly under observation, as in occasional cases of acute or subacute rheumatic carditis during convalescence occasional cases of congestive failure, from any

cause, under treatment with rest and digitalis, cases of anemia under specific therapy some cases of hypertensive heart disease treated by thoracolumbar sympathectomy and cases of the myxedema heart under thyroid therapy.

Hypertrophy and dilatation. The largest hearts are usually the heaviest hearts since hypertrophy and dilatation are almost invariably associated, and when a heart is so large that it reaches almost to the chest wall on the left and considerably over halfway to that on the right it will be found in the adult to weigh from 500 to 1 000 gm.

A few instances occur in which a single chamber is much dilated this is almost always the left atrium, which in cases of mitral valve deformity with atrial fibrillation may become enormous, large enough to hold a liter and a half of fluid or more and to fill a large part of the thoracic cavity extending across the mediastinal space to the right as well as to the left. The left atrium may be much larger than all the rest of the heart, which is attached to the atrium like an appendage the term "aneurysm of the atrium" has been applied to such cases. Both atria may be greatly increased in volume, as shown in Figures 120 121 and 122. The enlargement is almost wholly due to a stretching of the atrial wall, but the muscle is somewhat thickened also. The largest left atrium on record is said to have had a capacity of 3 liters (Minkowski, 1904) I have encountered one holding 1 760 cc (Figures 121 and 122) there are records of two other left atria larger than this, 2½ liters (Müller 1905) and 2 liters (Goedel, 1929)

The heaviest heart—cor bovinum found with marked aortic regurgitation or stenosis, or extreme hypertension of long standing—may weigh as much as 1 000 gm, over three times the normal. The heaviest heart recorded is said to have weighed 58 ⅛ oz (1 755 gm) and showed aortic and mitral valvular disease and a moderate degree of adhesive pericarditis of rheumatic origin in a man 28 years old (Smith 1850) the heart referred to above with the enormous left atrium pictured in Figures 121 and 122, weighed 850 gm and showed well-marked but not extreme mitral stenosis and regurgitation and very slight aortic stenosis.

Preponderant enlargement of either ventricle tends to give a rather characteristic shape to the heart like an egg with blunt end at the base of the heart in the case of a large left ventricle and more spherical in the case of a large right ventricle. The more hypertrophy and the less dilatation there are in left ventricular enlargement, the more the heart shape resembles that of preponderant right ventricular enlargement the more the dilatation of the left ventricle, the longer is the heart.

The factors responsible for enlargement of the left ventricle are as follows: for hypertrophy with little or no gross dilatation, uncomplicated chronic hypertension is mostly responsible and aortic stenosis occasionally (Figure 123 page 654) for dilatation with little or no hypertrophy there are serious acute myocarditis, as in some cases of rheumatic fever and diphtheria, acute myocardial infarction of large size, acute high-grade anemia and severe trauma for hypertrophy and dilatation, we may blame aortic regurgitation, mitral regurgitation,

chronic high-grade anemia, rarely chronic adhesive pericarditis, and most often left ventricular failure complicating chronic hypertension, aortic stenosis, and myocardial infarction from acute coronary occlusion.



FIG 120. Roentgenogram of thorax showing enormous heart shadow in a case of chronic rheumatic heart disease with mitral and tricuspid stenosis. Male, P W age 35 Note that the right heart border touches the right border of the thorax.

The factors responsible for enlargement of the right ventricle are as follows for hypertrophy with little or no gross dilatation, the most common cause is failure of the left ventricle without failure of the right, an occasional cause is mitral stenosis, and rare causes are extensive pulmonary fibrosis, pulmonary endarteritis, and congenital pulmonary stenosis (Figure 124 page 655) for dilatation with little or no hypertrophy we may find serious acute myocarditis, as in some cases of rheumatic fever and diphtheria, acute high-grade anemia, severe trauma, and acute massive obstruction in the pulmonary circulation from pulmonary embolism (acute cor pulmonale) for hypertrophy and dilatation, right ventricular failure complicating left ventricular failure is most

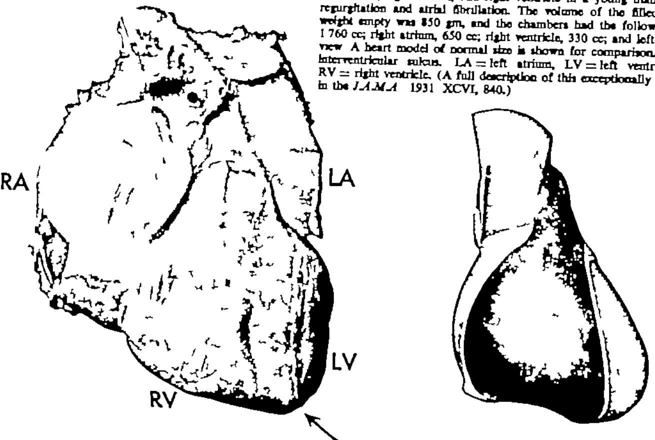


FIG. 121 Photograph showing marked enlargement of the heart due to dilatation of left atrium, right atrium, and right ventricle in a young man with mitral stenosis and regurgitation and atrial fibrillation. The volume of the filled heart was 4,600 cc, its weight empty was 850 gm, and the chambers had the following capacity left atrium, 1 760 cc; right atrium, 650 cc; right ventricle, 330 cc; and left ventricle, 70 cc. Anterior view A heart model of normal size is shown for comparison. The arrow points to the interventricular sulcus. LA = left atrium, LV = left ventricle, RA = right atrium, RV = right ventricle. (A full description of this exceptionally large heart was published in the *J.A.M.A* 1931 XCVI, 840.)



A



B

FIG. 122. Right lateral (*A*) and left lateral (*B*) views of heart shown in Figure 121 Note backward bulging of the left atrium best seen in the left lateral view LA = left atrium, RA = right atrium, LV = left ventricle, RV = right ventricle

commonly the cause, with mitral stenosis, pulmonary stenosis, and the chronic cor pulmonale as occasional factors, and less often tricuspid valve disease, chronic high-grade anemia, chronic severe thyrotoxicosis, congenital idiopathic hypertrophy and pulmonary regurgitation.

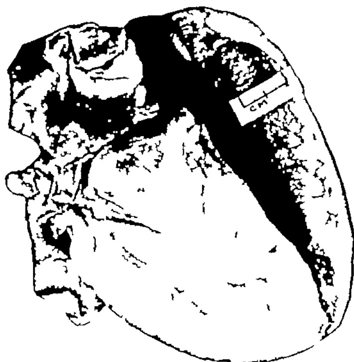


FIG. 1-3 Photograph showing a heart with much hypertrophied left ventricle (in case of aortic stenosis) The left ventricular wall measured cm in thickness (normally *1 0 to 1 cm*)

It is evident that several factors act simultaneously on both ventricles to *cause acute dilatation and chronic dilatation and hypertrophy* but uncomplicated hypertrophy of either ventricle is independent of the other when hypertrophy of the right ventricle follows hypertrophy of the left ventricle there is always an essential element of dilatation of the left ventricle as a part of the sequence.

Enlargement of the left atrium is chiefly the result of dilatation and occurs most markedly with mitral valve disease but also often with failure of the left ventricle. Similarly *enlargement of the right atrium* is chiefly due to dilatation and results from tricuspid valve disease or much more commonly from failure of the right ventricle.

Finally interesting but rare types of general cardiac enlargement are those found in infancy and once called congenital idiopathic hypertrophy Cases of glycogen storage (von Gierke s) disease (von Gierke, 1929 Pompe, 1933) of myocarditis of unknown cause, of coronary anomalies, and of excessively

rapid rates in paroxysmal tachycardia (Hubbard, 1941) have lately been separated out, leaving only a minority now unexplained. The heart weights in these various conditions are often several times the normal (Figure 74 page 324) and the prognosis is bad, except in the cases of tachycardia which recover when properly treated.

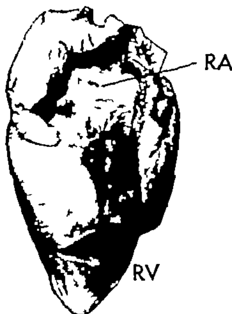


FIG. 124. Photograph showing marked right ventricular hypertrophy in chronic cor pulmonale; M.C., male, age 29 Three years after beginning of exposure to silica dust in gritty-soap factory Death due to complicating pneumonia. RA = right atrium, RV = right ventricle. (Kindness of Oxford University Press; chapter by P D White on Cor Pulmonale.)

MYOCARDIAL DEGENERATION AND FIBROSIS. CARDIAC RUPTURE. CARDIAC ANEURYSM. CALCIFICATION

Myocardial degeneration and fibrosis result chiefly from extensive coronary atherosclerosis with obstruction to the blood supply of the myocardium If the deficiency is gradual in its progress, so is the myocardial change which begins as scattered or local fatty degeneration and necrosis and ends in replacement of a certain number of muscle fibers by connective tissue (fibrosis) or in some slight degree of regeneration of muscle if the blood supply is soon enough re-established by collateral circulation. If the deficiency is abrupt and extensive in the amount of muscle involved, an infarct results which may heal as a firm scar (see Figures 106A, 106B and 107 pages 532, 533 and 535) or may proceed to aneurysm or rupture of the heart wall

Myocardial necrosis and fibrosis can also result from other causes than coronary atherosclerosis, though less commonly Syphilitic or embolic (chiefly

by bacterial vegetations) occlusion of the coronary mouths, and high degrees of aortic stenosis also, may rarely produce such lesions three cases of myocardial infarction due to syphilitic stenosis of the coronary ostia among 6,225 consecutive autopsies in New Orleans have been recently reported (Burch and Winsor 1942) Disseminated areas of ischemic necrosis may result from carbon monoxide poisoning or very severe anemia (Friedberg and Horn, 1939) and Davies (1948) has described endomyocardial necrosis and fibrosis in Africans.

Cardiac aneurysm and rupture, long recognized pathologically have only in recent years been properly attributed in the great majority of cases to coronary thrombosis with myocardial infarction. Both cardiac aneurysm and rupture are as a rule only postmortem findings, unrecognized for the most part before autopsy although they have been diagnosed in an increasing number of cases of late, especially cardiac aneurysm by the aid of roentgenology (Figure 125)

Rupture of the heart usually occurs a few days after acute myocardial infarction sets in, due to friability of the heart wall. Among 25 000 autopsies at the Los Angeles County Hospital from 1924 to 1941 there were 865 cases of unhealed myocardial infarction 72 of these (or 8 per cent) showed cardiac rupture, 13 involving the septum (Edmondson and Hoxie, 1942) the threat of such an accident is a very potent reason for insistence on absolute rest during the first fortnight after acute coronary occlusion. In a series of 22 mentally ill patients with acute myocardial infarction, 20 of which were clinically undiagnosed and hence untreated, rupture of the heart caused death in 16 (73 per cent) (Jetter and White, 1944) In contrast to the average findings of 5 to 10 per cent in the wards of a general hospital, as further exemplified by a series of 10 cases of cardiac rupture (9 5 per cent) among 105 patients with acute myocardial infarction (Friedman and White, 1944) Rupture rarely if ever occurs in cases of chronic or healed myocardial infarction it was found in none of 165 such cases in Friedman and White s series. It takes place within the first two weeks of the infarction, most commonly at the end of the first week. Cardiac rupture usually ends in instantaneous death but in some cases when the tear in the wall is small and the intrapericardial leak of blood gradual, death may be postponed for hours, finally resulting from hemopericardial tamponade (see Chapter 27) unless relieved by paracentesis, not a likely procedure in such cases. Cardiac rupture may rarely result from gumma, pyogenic abscess, tuberculous lesion, echinococcus cyst, malignancy and trauma. Rupture of papillary muscles and interventricular septum may also occur spontaneously in fresh myocardial infarction.

Cardiac aneurysm in slight degree is very common in fact it is present in nearly every case of extensive myocardial infarction. When aneurysms of the heart were first described several centuries ago they referred to general enlargement of the heart or of its chambers but in recent years the term has been reserved for local pouches or sacs in the heart wall. The cardiac aneurysm begins as an acute lesion and if no rupture occurs it becomes chronic with little or no danger of rupture after the first fortnight; it varies in size from a

slight bulge of the wall to an enormous cavity as large as the rest of the heart. Sometimes it contains a thrombus which may send off emboli. The aneurysm is located as a rule either on the anterior and left wall of the left ventricle near the apex, frequently involving a bit of the lower part of the interventricular septum (Figure 106A, page 532) or on the posterior wall of the left ventricle high up. These two sites are the usual locations of cardiac infarcts, due most commonly to occlusion of the descending branch of the left coronary artery in the one case and to occlusion of the right coronary artery or the circumflex branch of the left in the other case. Other but rare locations of cardiac aneurysms are the upper part of the interventricular septum, where the aneurysm may be also of congenital origin, and the outer wall of the right ventricle. Most

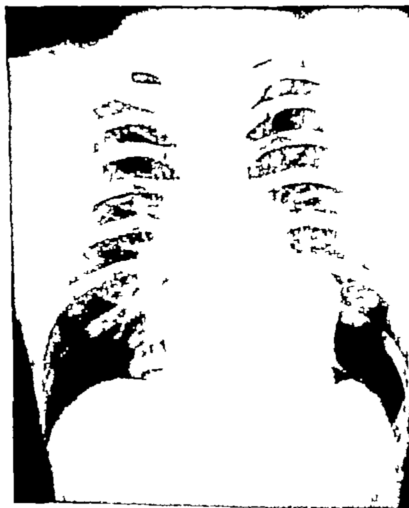


FIG. 125 Roentgenogram of thorax showing cardiac aneurysm consequent to myocardial infarction. H. O'D male, age 39 (Kindness of Dr A. N Ferguson, Fort Wayne, Ind.)

cardiac aneurysms are small or shallow and undiagnosable in life the largest ones are easily diagnosed by roentgen ray appearing as a bulge at the left border of the heart above the apex in the usual anteroposterior view and showing often an alarming but apparently benign degree of expansile pulsation during systole (Figure 125 page 657)

Marked dilatation of either atrium, especially of the left, has been called "aneurysmal," but this is a general and not a localized enlargement. Aneurysmal pockets in valve cusps and sinuses of Valsalva have also been described, due usually to bacterial endocarditis and rarely to congenital defects. There is no special treatment for cardiac or valvular aneurysms, except that strain on the heart should be carefully limited.

The deposition of lime salts in the heart muscle (calcification) is occasionally found, chiefly where there has already been myocardial disease, particularly degeneration following infarction from coronary closure. There is a disturbed local metabolism in such cases as there is at the base of the heart valves at times and in chronic valvular lesions with calcification of the cusps in whole or in part. The lime salts are most often found in the papillary muscles of the left ventricle or in the septum or anterior wall near the apex of the left ventricle. Irregular areas of calcification occur varying in size from that of a pea to that of a walnut. They may cast a shadow by roentgen ray which distinguishes them from the heart muscle about them. A cardiac aneurysm may be outlined roentgenologically by calcification of its wall. In very rare cases actual bone is found instead of mere masses of lime salts.

MYOCARDITIS

Myocarditis, or true inflammation of the myocardium occurs in rheumatic fever and in severe cases of diphtheria, infrequently in cardiovascular syphilis, and rarely in other infections like virus and rickettsial diseases (except in scrub typhus, tsutsugamushu fever when it is more common) typhoid fever, tuberculosis, trichiniasis, trypanosomiasis, hydatid disease and pyemia (see Chapters 14 16 and 17) It can be diagnosed clinically only by the realization of the frequency of mild to moderate involvement of the myocardium in these infections and in a few cases circumstantially by the finding of acute heart block, abnormal electrocardiograms, or acute cardiac dilatation without definite valvular lesions, coronary disease, or hypertension to account for the dilatation. In an analysis of 1 402 cases of myocarditis diagnosed post mortem, Gore and Saphir (1947) have presented a number of interesting ratios of the incidence of this condition in various diseases. Some of these ratios, where more or less adequate numbers of cases were involved, are as follows myocarditis was found in 144 of 221 cases of diphtheria, 5 of 135 cases of malaria, 9 of 581 cases of tuberculosis, 2 of 66 cases of syphilis, 5 of 41 cases of schistosomiasis, 1 of 400 cases of epidemic hepatitis, 32 of 222 cases of virus pneumonia, 13 of 144 cases of acute encephalitis, 13 of 94 cases of poliomyelitis, 11 of 48 cases of coccidioidomycosis 1 of 16 cases of tularemia, 14

of 160 cases of acute glomerulonephritis, 7 of 44 cases of exfoliative dermatitis, and 3 of 12 cases of Boeck's sarcoid. The discussion of the various etiologic types of myocarditis has been included in detail in appropriate chapters in Part II of this book.

There are in addition three kinds of myocarditis of unknown cause one occurring in earliest infancy in fact probably in fetal life to give rise to one type of congenital cardiac hypertrophy (Kugel and Stoloff, 1933) a second, called Fiedler's isolated myocarditis and acute interstitial myocarditis, of rare and obscure nature with tendency to sudden death to be further discussed below and a third, also obscure and rare occurring in variable degree in adults with cardiac enlargement which leads to congestive failure or sudden death (Levy and von Glahn, 1937) Whether or not these three groups are related as varying results of the same underlying condition is not known.

The clinical diagnosis of "myocarditis, so freely used in the past, has wrongly included many other conditions, in particular the frequent instances of hypertensive heart disease in which there is cardiac hypertrophy and enlargement but no inflammatory reaction in the muscle the term "myocarditis" has also wrongly included frequent instances of coronary heart disease, in which degenerative changes, fibrosis, and atrophy may occur without actual inflammatory process. In the attempt to diagnose heart disease more accurately the term myocarditis is wisely being abandoned in large part, we must remember nevertheless that there does exist such a condition as myocarditis which is in particular exemplified by involvement by rheumatic fever and diphtheria.

FIEDLER'S MYOCARDITIS

In 1899 there was published in the *Festschrift zur Feier des funfzigjahrigen Bestehens des Stadtkrankenhauses zu Dresden-Friedrichstadt* a paper of sixteen pages entitled "Ueber akute interstitielle Myokarditis" (Concerning Acute Interstitial Myocarditis) by Dr. A. Fiedler chief physician to the City Hospital at Dresden. Quotations from this interesting paper are as follows (translation by myself)

"Based on the clinical records and autopsy findings of four cases who died and on the record of an additional patient who survived the disease, there has been presented herewith the description of an acute inflammation of the myocardium, generally coming on very abruptly and with a chill, which is almost certainly of microparasitic origin.

"This disease attacks as a rule young people and runs its course with little or no fever The pulse rate is almost always very much accelerated and very rarely reduced. The heart is dilated both to right and to left. The heart action is irregular and dyspnea, cyanosis, evidences of stasis in both greater and lesser circulations, and a great tendency to heart weakness are constantly present.

"I cannot convince myself that we are dealing in these cases with an ordinary septic infection. To my mind it is much more evident that a microorganism, differ

ent from the usual agents producing sepsis, is responsible, localized directly in the heart muscle and setting up there an inflammatory reaction or that a poison is produced which reaches the heart by the blood stream and affects particularly the interfibrillary tissue of the myocardium.

In diphtheria, scarlet fever and exanthematic typhus, that is, in diseases which are caused by entirely different infectious agents and which differ also so widely in their clinical manifestations, we find, as mentioned above, interstitial myocardial changes very similar to those in the cases which I have observed and described herein.

"We may conclude that in all these different diseases one and the same poison does not produce these myocardial changes but that entirely different infectious agents are present which cause this inflammation either directly or indirectly.

I would not fail to mention that even though interstitial myocarditis is always preponderant this designation is not to be accepted in the strictest and exclusive sense of the word. The interstitial changes in the muscular tissue were the first and most important but, as microscopic investigation showed, there was also always present a parenchymatous inflammation too consisting of slight changes in the muscle fibres themselves.

And now still a few words about the prognosis of the disease in question; as mentioned above, our cases ended as a rule fatally. This does not, however, force the conclusion that all of these cases have a bad prognosis.

Microscopic sections of the myocardium in those cases who survived only a few days after the onset of chill and serious illness showed invasion of the myocardium with small round cells and beginning disintegration of the myocardial fibers.

Therefore, the designation of this disease as purely interstitial (or isolated) is misleading. One might better term it acute myocarditis of unknown cause *although there is no reason why one may not add "Fiedler's type" in parenthesis* after such a description. It is quite possible that an acute fulminating virus myocarditis may be the answer. If the etiologic factor is evident it should be so stated and the designation "Fiedler's" omitted. In time all such cases may be separated off from the one-time useful eponym.

ATROPHY OF THE HEART MICROCARDIA

Atrophy may be dismissed with two observations. (1) When relative disuse or inanition or Addison's disease is responsible for the atrophy the heart actually decreases somewhat in bulk and weight, in whole or in part, with slight decrease in size of the muscle fibers; such atrophy is infrequent and slight in most cases. Atrophy is sometimes seen in the left ventricle in well-marked mitral stenosis and in the whole heart in a few cases of chronic constrictive pericarditis, and in bedridden patients, as in chronic tuberculosis. Marked atrophy of the left ventricle has been produced in the experimental animal by an artificial tricuspid valve lesion (Stadler 1907). (2) If degeneration or inflammation causes local atrophy partial fibrosis results, but the heart as a

whole does not decrease in size or weight if it must still keep up an active circulation, in fact there may develop a compensatory hypertrophy

True microcardia, if it exists, must be very rare It has been reported as a congenital anomaly at birth, but further confirmation is necessary

TOXIC AND MALNUTRITIONAL MYOCARDIAL CHANGES

In rare cases there are myocardial changes of noninfectious toxic origin and others associated with malnutrition and avitaminosis (see Chapter 23) Chloroform, carbon monoxide, benzol, and the toxins of eclampsia and uremia have been noted as factors responsible for focal necroses and severe malnutrition with vitamin deficiency as in beriberi and rachitis, has occasionally caused myocardial degeneration and edema with dilatation of the heart. Upon specific therapy both the general malnutritional edema and the cardiac dilatation tend to subside It is thought that in especially severe cases in children congestive heart failure may supervene to cause death (Waring, Charleston S. C. personal communication, 1936) In scorbutus, hemorrhages may occur throughout the heart. As a matter of fact avitaminosis tends to be multiple and therefore to show multiple effects, both generally and in the heart.

Sensitivity to the sulfonamides has also been reported as a cause of damage to the myocardium which may be reversible (Lilienfeld, et al. 1950· Mayer and Levy 1950)

FATTY DEGENERATION IN SEVERE ANEMIA

Associated with the cardiac dilatation and hypertrophy that result from severe anemia there is a characteristic fatty degeneration of certain parts of the heart muscle farthest removed from the arterial ends of the capillaries, giving rise to a curious striped appearance which has occasioned the term "tiger" or "tiger-lily" heart. Otherwise fatty degeneration is but a part of the effect of severe infections like diphtheria, or of infarction due to serious coronary disease.

FATTY INFILTRATION

Fatty infiltration of the myocardium, especially involving the right ventricle is a definite entity most common in middle-aged and elderly women. In extreme cases the wall of the right ventricle is found largely composed of layers of fat infiltrated between the muscle bands. In rare cases this condition has been blamed as the primary or secondary cause of heart failure. When excessive it may be merely a part of generalized fatty infiltration in other organs and throughout the body

AMYLOID DISEASE. XANTHOMA. HEMOCHROMATOSIS. SARCOIDOSIS

Rare affections of the myocardium of obscure origin include amyloid disease, xanthoma, hemachromatosis, and sarcoidosis, which tend to be but part

of a general process of amyloid, xanthomatous, and iron deposition, and mucoid infiltration throughout the body (see Chapter 23) When such processes have become evident elsewhere, as, for example, in the skin, and the heart is enlarged or in other respects abnormal, showing, for instance, otherwise unexplained heart block by electrocardiogram, it is reasonable to suspect that these diseases have involved the heart.

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CHAPTER 26

ENDOCARDIAL AND VALVULAR DISEASE INTRACARDIAC THROMBOSIS

Endocardial disease is chiefly a matter of endocarditis, but it includes also infarction (incident to coronary thrombosis) atheroma, neoplasm, and trauma of the endocardium.

ENDOCARDITIS

Endocarditis, or inflammation of the endocardium, is made up of several types varying according to the etiologic factors. These etiologic types have been described in detail in Chapters 14 15 16, and 17 of this book and will be but briefly summarized here They are the rheumatic," subacute bacterial, *acute bacterial, terminal verrucose, syphilitic,* tuberculous, and other infectious types.

The *rheumatic" endocardial involvement* is a simple verrucose lesion with rows of small vegetations or thrombi, consisting mostly of fibrin, on the valves, often located only along the line of closure of the mitral cusps but sometimes *situated* on other heart valves, also where they close (Figure 83 page 362) on the chordae tendineae, and on the atrial mural endocardium. Recovery may be complete without deformity and with but little thickening *of* the valve leaflets, but more often there is extensive scarring with contraction and adhesion of the cusps and of the chordae tendineae causing stenosis and regurgitation, especially after repeated rheumatic infections. This type of acute endocarditis is rare before the age of 5 years and relatively uncommon after 15

The *subacute bacterial endocardial involvement* consists primarily of a lesion of the valves with larger vegetations than in the case of rheumatic endocarditis and with more extensive infection of the mural endocardium of atria and of ventricles, due to extension of the process from the valves or to contact with infected cusps (Figure 88 page 393) The vegetations contain masses of bacteria, usually streptococci of the viridans type or products of their degeneration. Chronic healed scarring and deformity are now the rule in subacute bacterial endocarditis because of the lowered mortality from this disease by the use of penicillin in the active stage. Rupture of valve cusps and chordae

tendineae occasionally occurs, and embolism from the endocardial vegetations is very common. This type of endocarditis is commonest between the ages of 18 and 35 years but may occur at any age thereafter or less commonly earlier.

The *acute bacterial endocarditis* is much like the subacute bacterial type except that it is a more fulminating process and now becoming rare. It is caused by any one of a variety of organisms, most commonly by streptococcus, pneumococcus, staphylococcus, or gonococcus.

Terminal verrucose endocarditis resembles the rheumatic type. It is quite common as a complication of many fatal illnesses. It is probable that a nonrheumatic verrucose endocarditis can occur in many patients who recover, leaving slightly thickened cusps difficult to distinguish from very mild chronic rheumatic endocarditis, but of that we have not yet clear proof

Syphilitic involvement of the endocardium is due to an extension of syphilitic aortitis to the aortic valve causing an adhesion of the cusp ends against the aortic wall, which results primarily in a widening of the commissures and secondarily thereby in aortic regurgitation. It should be noted, however that the wall of the very first portion of the ascending aorta may be so weakened by the syphilitic process that it dilates, and that therefore this dilatation, rather than aortic valvular disease, may be responsible for some of the widening of the aortic valve commissures and of the resultant aortic regurgitation. Further extension of the syphilitic process from the aortic valve may slightly involve the anterior cusp of the mitral valve.

Tuberculous endocarditis consists of the involvement of the endocardium by military tubercles with or without ulceration. It is rare.

Also rare are other infections like actinomycosis and extension to the endocardium of myocardial abscesses.

Combined lesions are frequently found and it is sometimes possible to determine in the pathologic specimens the effect of each individual factor

OTHER ABNORMALITIES OF THE ENDOCARDIUM

Other abnormalities of the endocardium include a variety of conditions. Frequently there are unimportant *atheromatous* lesions of the valvular or nonvalvular (mural) endocardium which are similar to areas with early fatty changes in the aorta and coronary arteries, but the endocardial lesions progress only rarely to clacified plaques. In some cases with extensive subendocardial calcification the endocardium may be eroded by direct pressure. Occasionally the destructive process associated with myocardial infarction from coronary thrombosis or embolism penetrates to the endocardium to cause ulceration and intracardiac thrombosis over the site of the ulceration. *Mural thrombosis* may however and probably most commonly does, develop as the result of stasis rather than of endocardial injury especially in a fibrillating atrium or in a ventricular (as in an aortic) aneurysm. *Neoplasm* and *trauma of the endocardium are rare* (see Chapter 23) as are also *congenital valvular defects* (see Chapter 13) *Diffuse parietal endocardial sclerosis* occurs in rare cases, most

commonly in congenital heart disease its pathogenesis is still obscure. *Endocardial and subendocardial calcification* is, however very frequent and consists of two types, the more common being superimposed on old valvular disease, mainly rheumatic, and the other (Mönckeberg's sclerosis) being an independent atherosclerotic process which attacks especially the valve rings and bases but may also invade the cusps. It is important to note that chronic endocarditis with extensive valvular deformity may exist, even in old age, with little or no calcification, and that much calcification may occur with little or no evidence of antecedent endocarditis, although both processes are, to be sure, frequently combined, the old endocardial scarring doubtless favoring the calcification. An interesting, very rare, dark brown pigmentation (ochronosis) of heart valves, aorta, cartilage, and bone has been ascribed to an "inborn fault of tyrosin metabolism" (Neumann, Brno 1946) Finally *endocardial fibrosis* of unknown origin has been described in Africans by Davies (1948)

VALVULAR DISEASE OF THE HEART

Valvular disease of the heart is an important subject for consideration not only because it is often the primary cause of heart failure, but also because there is much unnecessary confusion associated with it in the medical literature and in the minds of many physicians As noted in Chapter 14 valvular disease is a common structural abnormality wherever the rheumatic infection is frequent, it must, however be distinguished from valvular incompetence due to cardiac dilatation alone

Valvular disease is caused by acute infection, which includes the rheumatic (most commonly) subacute bacterial, acute bacterial, and terminal verrucose types by syphilitic invasion, and rarely by tuberculosis it is sometimes due also to atheromatous and sclerotic changes, often with calcification, chiefly at the base of the aortic valve, without any evidence of infection uncommonly it is due to congenital malformation rarely it is due to trauma, either direct or indirect. There may be an acute fulminating or terminal involvement, or the process may be very chronic, consisting of a healed after-effect of some acute process that occurred many years before. Often two factors are combined, for example subacute bacterial endocarditis superimposed on congenital defects or on chronic rheumatic valvular disease, calcification of valves already deformed by infection, or rupture of inflamed valves

Valvular disease may be so slight that there is not enough deformity to interfere in any way with the valve function, in such cases there may be an entire absence of signs and symptoms. On the other hand, the valvular defect may be so great that it is itself the cause of much cardiac enlargement and failure Even with objective signs of valvular deformity there may be no disability and life may extend to a ripe old age, as in the case of Dr Herman F Vickery who lived to be nearly 84 with a moderate degree of "rheumatic" mitral stenosis in addition to some coronary insufficiency (White and Bland, 1941) A coincidence of coronary heart disease and chronic rheumatic heart

disease is more common than generally recognized (Gardner and White, 1949)

It is important always to distinguish between the influence of active disease and that of structural abnormality on the circulation and health. For example, acute bacterial endocarditis may show but little valve deformity and yet terminate fatally in a short time because of the toxic effect of the infection or of embolism, while chronic mitral stenosis or aortic regurgitation of rheumatic origin though of high degree may allow many years of life with a badly crippled heart. An abnormal valve, no matter how slight its deformity is always of some significance because it is a point of less resistance to infection or stress than is a normal valve and sometimes it is but a part of some important acute or chronic disease. These facts are frequently lost sight of in the casual disregard of valvular disease which has been common in the past.

Clinically it is often difficult or even impossible to say whether valvular insufficiency is due to disease of the valve itself or to cardiac dilatation with normal valve or to cardiac dilatation plus valvular disease. Sometimes it is easy to make the differentiation, but in certain cases, especially in those with advanced heart failure, we may utilize without avail all methods of study including percussion, auscultation, sphygmomanometry roentgenology and graphic methods In most cases of advanced heart failure it matters little whether the valves are diseased or not, so far as prognosis and treatment are concerned. It is in the earlier cases without congestive failure and with relatively little cardiac enlargement that the differentiation between valvular disease and functional defect alone is much more important and is often possible. All methods of examination are sometimes needed in this differentiation; one method alone, like auscultation or roentgenology may be misleading.

Of the four heart valves the mitral is the one most commonly affected it is damaged in well over half of all cases of valvular disease. Aortic valve disease is next in frequency followed by lesions of the tricuspid valve, which is but rarely deformed to any important extent. The pulmonary valve is very infrequently involved. In a series of 208 cases of valvular disease in New England examined macroscopically post mortem the mitral valve was found diseased in 85 6 per cent, the aortic valve in 44 7 per cent, the tricuspid valve in 15 9 per cent, and the pulmonary valve in 1 9 per cent (Cabot, 1926) The aortic and mitral valves were involved together in 19 2 per cent, the aortic, mitral, and tricuspid in 11 per cent, the mitral and tricuspid in 2.9 per cent, the pulmonary and tricuspid in 1 per cent, and all four valves in 1 per cent. In a postmortem series of 126 cases of valvular disease studied in Vienna the percentages of disease of mitral, aortic, tricuspid, and pulmonary valves were 60, 76, 25 and 0 respectively (Kaufmann, 1927) but these patients were all male adults and syphilis accounted for one third of the aortic valve lesions. In a series of 300 autopsied cases of valvular heart disease in Berlin (Sperling, 1872) the mitral valve was involved in 85 per cent of all cases and in 52 per cent without other valves affected, the aortic valve was involved in 43 per cent altogether and alone in 13 per cent, the tricuspid valve in 10 per cent altogether but

alone in only 1 per cent, while the pulmonary valve was diseased in only 1 per cent of the total cases and in no case alone. In a series of 1 097 cases in New England in which valvular disease was sufficient or definite enough to be diagnosed clinically 56.3 per cent were thought to have mitral valve disease alone, 14 7 per cent aortic alone, and 28 9 per cent both aortic and mitral, rare cases were thought to have tricuspid valve disease along with mitral disease or with mitral and aortic, but in no case of the series was tricuspid valve disease a certainty pulmonary valve disease was diagnosed in no case (White and Jones, 1928) In a clinical series of 1 781 cases of valvular disease at the Johns Hopkins Hospital (Hirschfelder 1918) mitral valve disease alone was diagnosed in 51 per cent, aortic valve disease alone in 22 per cent, and both together in 20 per cent. Why the mitral valve should be most often involved and why the left heart valves are more frequently diseased than those on the right side is not clear Greater vascularity of the mitral valve has been suggested as a cause, but it is probable that the greater force of closure of the mitral and aortic valves allows more readily a lesion produced by direct or indirect bacterial action combined with trauma at their lines of closure than in the case of the right heart valves which are under less pressure, except in fetal life when the pulmonary and tricuspid valves are more often involved than the aortic and mitral valves.

The characteristics of the individual valve lesions will now be considered in the order of frequency of valvular involvement mitral, aortic, tricuspid, and pulmonary

A. MITRAL VALVE DISEASE

Disease of the mitral valve is common but it is frequently diagnosed when not present, because a systolic murmur at the cardiac apex due to cardiac dilatation is wrongly interpreted as due to valvular disease

Etiology *Cause* Mitral disease is due in the large majority of cases to rheumatic infection. It may be found either in the acute stage or as a chronic lesion. In the acute stage the rheumatic infection may not be recognized as such, either because it gives very obscure or indefinite signs, or because no doctor is called at the time, or because the doctor who is called is unfamiliar with atypical rheumatism, but the resulting heart involvement is generally regarded as rheumatic and is called the rheumatic type," probably justifiably It is possible that other infections, especially of focal nature, may be some times responsible, but this still remains to be proved. Subacute and acute bacterial endocarditis are much less frequent causes of mitral disease and until lately were always fatal. Terminal verrucose endocarditis as a complication is not infrequently found in patients who have died from all kinds of diseases it involves the mitral valve most commonly Atheromatous lesions in the mitral valve are very similar to early atheromatous lesions of the blood vessels they consist of the infiltration and precipitation of lipoids, cholesterin crystals, and calcium in the leaflets on their ventricular sides, suggesting the

importance of mechanical factors (Hellwig, 1942) Sclerotic change with calcification at the base of the valve sometimes fixing the annulus as a solid stony ring is infrequently encountered when calcification involves the mitral valve leaflets themselves it is almost invariably superimposed upon antecedent rheumatic mitral stenosis, in which case it may further deform the valve, sometimes with masses of calcium projecting into heart chambers or even into the atrioventricular ostium to increase the degree of stenosis. Tuberculous and syphilitic involvement are very rare, as is also congenital deformity in the nature of either stenosis or atresia.

Age Mitral valve disease is commonly found in youth and middle age; it is less common in old age, although both the rheumatic and the sclerotic types are found in old persons In infancy mitral valve disease is very rare.

Sex. The female sex shows a higher percentage of mitral valve disease than does the male, in about the ratio of three to two.

Pathology Although the pathology of endocardial disease, whether of inflammatory atherosclerotic, or traumatic nature, has already been discussed in the earlier part of this chapter and in Chapters 14 15 and 16, the particular pathology of chronic mitral disease needs brief consideration. The healing of acute endocarditis may leave no defect in valve function and merely a slight thickening of the valve cusps along their lines of closure. With marked or repeated inflammation the damage is greater and the contracting scar tissue may cause all grades of deformity Two processes in particular are responsible for defective function one of these is fusion of the cusps at their commissures causing both stenosis (narrowing of the ostium or opening) and regurgitation (leaking back of the blood stream through the incompetent valve) the other is fusion of the chordae tendineae, with shortening, which is equally important in deforming the valve. In very chronic cases after repeated infections the fusion of the cusps is so pronounced that there is simply a diaphragm or funnel with a narrow ostium in the place where the freely acting mitral cusps should be (Figure 126) The small opening varies in shape and size and it has received a variety of names such as "buttonhole" and "fish mouth." Occasionally the damaged valve becomes calcified and absolutely rigid, with stony surface exposed to the blood stream through erosion of the endocardium. A few instances occur in which a valve cusp is rent or a chorda tendinea torn off its attachment at one end so that the torn fragments float freely at one end or edge in the blood stream. The valve ring at its base and sometimes the valve cusps themselves to a greater or lesser extent may become calcified and fixed, with more or less stenosis. Large vegetations in bacterial endocarditis may sometimes produce a virtual mitral stenosis without actual valve deformity Finally developmental defects and probably infectious lesions may give rise in the fetus to stenosis, hypoplasia, or even atresia of the mitral valve.

Mitral regurgitation and mitral stenosis are almost invariably combined pathologically In rare instances, however they may be considered pure (1) when retraction of the relatively undamaged or at least relatively nonadherent valve cusps is caused by shortened, contracted, and perhaps fused

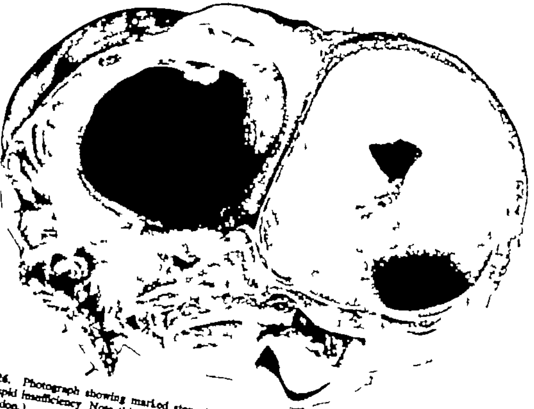


FIG. 126. Photograph showing marked stenosis of the mitral ostium with fish-mouth valve and relative tricuspid insufficiency Note thick wall of left atrium. (Kindness of Dr Ronald Grant, Guy's Hospital, London.)

chordae tendineae giving rise to mitral regurgitation without stenosis, and (2) when the valve cusps are fused giving rise to mitral stenosis without sufficient fibrosis or thickening of the cusp extremities or shortening of the chordae tendineae to allow regurgitation. When the valve opening is rigidly fixed with fibrous or calcified edge in marked mitral stenosis a certain amount of regurgitation necessarily occurs too Clinically preponderant mitral stenosis produces a different picture from that of preponderant mitral regurgitation and when the two defects are about balanced the clinical findings show the combined effects of moderate mitral stenosis and moderate mitral regurgitation. From the pathologic point of view it would be more accurate to make a clinical diagnosis of "mitral disease with preponderant stenosis" or "with preponderant regurgitation" but the shorter terms mitral stenosis and "mitral regurgitation" are much simpler for use and sufficiently accurate if we realize that they refer to the clinical results of preponderant defects of the mitral valve

Functional mitral insufficiency due to left ventricular dilatation should not be regarded as a trivial condition. Often the left ventricular dilatation is the result of serious myocardial disease itself, of infarction, for example, or of left ventricular failure due to the strain of hypertension, or of myocardial insufficiency because of serious anemia It may be due to adhesive pericarditis or it may be a compensatory mechanism with aortic regurgitation. It is possible that the displacement downward of the papillary muscles as the result of the ventricular dilatation is a more important factor in causing the mitral regurgitation than is dilatation of the atrioventricular ostium, that is, of the valve ring. The chordae tendineae are of limited length and with their attachments to the papillary muscles moved away from the base of the heart their insertions on the valve cusps are likewise displaced downward. This results in an inability of the mitral cusps to close tightly no matter how tautly the chordae may stretch or how normal or elastic the cusps may be regurgitation of greater or lesser degree follows. Occasionally in fact frequently factors due both to left ventricular dilatation and to deformities of valve cusps and chordae tendineae combine to cause mitral regurgitation.

Functional mitral stenosis occurs (a) occasionally as a relative stenosis with normal mitral valve but marked left ventricular dilatation, (b) in very rare instances of tumor or thrombus in the left atrium large and free enough to obstruct to a variable degree the blood flow through the mitral valve from atrium to ventricle, and (c) perhaps to a slight degree in marked aortic regurgitation when the aortic regurgitant blood stream forces back the anterior cusp of the mitral valve.

The average normal circumference of the mitral valve in the adult human heart is 10 cm (ranging from 9 to 11 cm) a circumference less than 7.5 cm may be considered to indicate definite stenosis. The area of the normal adult mitral ostium has a range during life of 4 to 6 sq cm An area of 1 sq cm or less is found in the case of marked mitral stenosis (Gorlin and Haynes, 1950)

Effects of mitral valve disease on the heart. If the mitral valve lesion results primarily in stenosis, the left atrium and right ventricle bear the brunt of the burden, the former becoming hypertrophied and dilated and the latter hypertrophied at first and finally dilated also, when the strain is much increased. Eventually the right atrium also is involved, with dilatation and hypertrophy after the right ventricular dilatation has resulted in more or less constant tricuspid regurgitation. The left ventricle may remain practically unaffected even when the right ventricle and left atrium become double their normal size. In fact the left ventricle may be a little smaller than normal. The cardiac apex is sometimes formed in large part by the right ventricle.

If, on the other hand, regurgitation is the chief defect, the left ventricle becomes involved as well as the left atrium and right ventricle. Hypertrophy and dilatation of left ventricle and left atrium and hypertrophy of the right ventricle are the primary effects, with dilatation of both right heart chambers later. With marked and chronic mitral regurgitation the heart may become enormous, all four chambers being involved. "Functional" mitral regurgitation will naturally have the same effect on the heart chambers as "organic" mitral regurgitation of the same degree and chronicity, but with functional mitral regurgitation other factors such as heart failure may cause death before enough time has elapsed to duplicate the picture found with organic mitral disease without failure at the onset, or recovery from the dilatation and failure (due to anemia or other factors responsible for the functional mitral regurgitation) may permit the valve again to become competent.

Since both defects—stenosis and regurgitation—are generally combined to a greater or lesser degree in cases of organic mitral disease, the effects on the heart depend in part on the relative amounts of stenosis and regurgitation and in part on the absolute degree of the valvular disease. With slight mitral regurgitation or stenosis there is scarcely any heart burden and but little change in heart size, but when either stenosis or regurgitation is extreme the changes are marked.

High grades of organic mitral stenosis are much more common than are high grades of organic mitral regurgitation and are doubtless better borne. The development of mitral stenosis is a gradual one, the earliest defect in rheumatic children being more regurgitant than stenotic. It requires at least two years as a rule for the establishment of mitral stenosis. Mitral murmurs heard during the first year after the onset of a moderate or severe rheumatic infection in a child are to be attributed to dilatation of the left ventricle incident to the rheumatic myocarditis and not to mitral valve deformity (Bland, White, and Jones, 1935); such murmurs may eventually merge into those of mitral valve disease or they may disappear occasionally when recovery is especially satisfactory (Bland, Jones, and White, 1936). The heart and body as a whole gradually develop compensatory mechanisms to take care of the strain of the stenosis, often for many years. The rather sudden onset of functional mitral regurgitation with heart failure or its more gradual develop-

ment with marked aortic regurgitation may however be a great additional burden for the heart and hasten its failure before a compensatory mechanism can be established.

A particular finding occasionally seen in mitral disease is an enormous enlargement of the left atrium. It is not alone the degree of stenosis that accounts for such cases but rather the combined effect of mitral regurgitation, mitral stenosis, the dilatation that comes with atrial fibrillation, acute rheumatic involvement of the myocardium of the left atrium and other factors not well understood, perhaps an active circulation or sometimes pericardial adhesions over the left atrium. In a series of 26 cases of very large left atria found at autopsy at the Massachusetts General Hospital, 16 showed mitral stenosis and 10 mitral valve deformity (causing regurgitation) without stenosis, which indicates that "structural" mitral regurgitation is by no means an innocuous condition.

The heart muscle in mitral valve disease may be normal except for hypertrophy With acute endocarditis there are often acute inflammatory myocardial reactions, like the Aschoff bodies in the rheumatic infection, but with chronic healed valvular disease there need not be any trace of previous infection in the perfectly healthy muscle. Eventually the myocardium may become exhausted and fail without evidence of pathologic change unless there is a complication such as acute rheumatic infection or serious coronary disease. Thus it is at times the valve lesion, and not myocardial disease that eventually causes failure and death, although it is equally true that active infection, especially recurrent rheumatism, or some other complication proves too great a burden for the heart that is already overloaded. In recent years there has been too great a tendency to blame the heart muscle entirely and to exonerate the valve lesion. This is a limited point of view although it has been helpful in calling attention to the fact that mitral insufficiency is often the result of heart failure or dilatation and not its cause. In the process of this demonstration the pendulum has swung too far The truth rests between the extreme points of view

The effects of mitral valve disease on organs of the body other than the heart vary with the degree of involvement of the valve and with the occurrence of complications. The only direct effect is on the pulmonary circulation which becomes engorged the small arteries and capillaries are seriously affected with marked dilatation and thickened walls resulting in great difficulty in the transfer of oxygen and carbon dioxide from the limited inspired air to blood stream and vice versa (Parker and Weiss, 1936) There develops a steadily increasing pulmonary arterial pressure when either stenosis or regurgitation of the mitral valve is at all pronounced. All this leads naturally to a diminution in air space and vital capacity and to a tendency to bleeding or effusion of serum (edema) into the interstitial tissue and into alveoli and bronchioles; there slowly develops also an extensive interstitial fibrosis with enormous thickening of the alveolar walls to resemble eventually the picture of "malignant pulmonary sclerosis due to other causes. Also in time in cases of

chronic mitral stenosis there may be laid down in the lung tissue iron deposits from the infiltration of blood, and these deposits may give rise to a characteristic x-ray picture of miliary pulmonary hemosiderosis. The liver becomes congested only when the right heart fails but such congestion over the years may lead to a moderate "cardiac cirrhosis" of the liver.

Symptoms. There are no symptoms of mitral valve disease except for evidence of the limited air space in the lungs in most cases. Dyspnea on effort is common when the mitral valve disease is more than slight in degree, while indication of a high degree of pulmonary engorgement from marked mitral stenosis is dyspnea even at rest, or in paroxysmal attacks (with or without acute pulmonary edema or cardiac asthma) when the heart rate suddenly increases. The dyspnea in mitral stenosis is not to be attributed to failure of the myocardium. It is due to the mechanical effect of the stenosed mitral valve. Cough and hoarseness due to the pressure from a very large left atrium are uncommon symptoms, as is also hemoptysis, due to "pulmonary apoplexy."

Vieussens, R. *Traité Nouveau de la Structure et des Causes du Mouvement Naturel du Coeur.* Jean Guillemette, Toulouse, 1715. pp. 105 and 106. (Translation by myself.)

"I perceived that the opening into the left ventricle appeared very small and was of an oblong oval shape, and in seeking the cause of such a surprising fact I discovered that the cusps of the mitral valve were truly bony and so thickened and contracted that they very much narrowed the ostium.

"The entrance into the left ventricle having been much narrowed and its margin having lost all its natural suppleness the blood could no longer enter so freely and abundantly as would be necessary into the cavity of this ventricle. In consequence of the embarrassment of the circulation the blood began to dilate extraordinarily the trunk of the pulmonary vein [that is, the left atrium] because it remained there so long and collected in such a great quantity. The blood had no sooner begun to make too long a stay in the main trunk of this vein than it delayed the course of blood in all the blood vessels of the lung, so that the branches of the pulmonary artery and vein extending throughout all the tissues of the lung were always too much filled with blood and consequently so dilated that they compressed the vesicles to such an extent as to hinder the air from entering and leaving freely: *that is why the patient breathed always with much difficulty.*" (Italics mine.)

Complications like congestive heart failure, atrial fibrillation, pulmonary embolism, massive left atrial enlargement, and acute rheumatic or bacterial endocarditis may produce symptoms which are discussed in the chapters in this book dealing with these subjects. Angina pectoris in mitral stenosis is rare, having been found in only 2.6 per cent of Levine and Kauver's 741 cases (1942) and then almost always due to an incidental complication of coronary heart disease; there were, however, three of these authors' cases of mitral stenosis with angina pectoris who showed no significant coronary artery disease, and these, plus a few others seen by ourselves and by other observers (Blackford, 1940; Dressler, 1942), indicate the probability that in rare cases

of marked mitral stenosis the output of blood from the heart may be inadequate to meet the needs of the coronary circulation on effort.

Signs. There are only two pathognomonic signs of mitral valve disease, one auscultatory and the other roentgenologic. Both show the presence of mitral stenosis. Mitral regurgitation due to valvular disease cannot be easily differentiated from mitral regurgitation due to ventricular dilatation except when it is combined with proof of mitral stenosis.

The auscultatory proof of mitral stenosis is the presence of a rumbling apical middiastolic murmur (Figure 15 page 95) with or without presystolic accentuation, in the absence of considerable aortic regurgitation or other cause of left ventricular dilatation. It was first recognized by C. J. B. Williams more than a century ago, but his description went unheeded until the present generation again called attention to it as an essentially diastolic and not merely a presystolic murmur

Williams, C. J. B. *Diseases of the Chest* John Churchill, Publisher London, 3d edition, 1835 p. 198

"*Mitral valve* Obstructive disease of this valve commonly consists in an adhesion together or ossification, or rigidity of some of its parts, or in a thickening and contraction of the fibrous ring at its base. It may cause a murmur with the diastole of the ventricle, and therefore, at the time of the 2nd sound, for although the ventricle in itself produces no sound, yet, when the orifice, by which it becomes refilled is contracted, the current being partially resisted in passing through, may become sonorous. This will therefore leave the result much as Laennec represented it, inasmuch as there is a current from the auricles to the ventricles during the diastole of the latter although this current is not produced as he supposed, by the contraction of the auricles. *But the results of my late experiments must modify* the statements of both M. Laennec, and Dr. Hope, in this respect, that the contraction of the mitral orifice with its impeded current and attendant murmur will not necessarily supplant the 2nd sound, inasmuch as this sound is seated in the semilunar valves, the action of which may still be perfect.

The roentgenologic proof of mitral stenosis is the presence of a considerable increase in the size of the shadows of the right ventricle and of the pulmonary artery combined with well-marked enlargement of the left atrial shadow or the latter finding with any type of ventricular enlargement, left, right, or combined (Figure 127). Given either or both of these auscultatory and roentgenologic findings, and they are usually combined, the presence of an apical systolic murmur means mitral regurgitation as well as mitral stenosis and is due to the valvular disease (provided a respiratory murmur can be excluded). A large left atrium raises the left bronchus.

Other signs strongly suggesting, though not proving, mitral disease include a loud apical systolic murmur without any diastolic murmur in the absence of any acute or subacute illness or of evidence of left ventricular enlargement. Appreciable left ventricular enlargement would of course indicate that the cause of such a murmur could well be ventricular dilatation. The history of



FIG. 127 Roentgenograms showing a heart with high degree of mitral stenosis, a big right ventricle, and marked enlargement of the left atrium, which bulges to the right above the right atrium in the anteroposterior view (*A*) and posteriorly into the shadow of the spine in the right anterior oblique view (*B*). Note the displacement of the barium-filled esophagus by the broad curve of the left atrium below the aortic and pulmonary artery notches, in the oblique view

rheumatic infection in the past makes this apical systolic murmur all the more important evidence of mitral disease.

Another corroborative sign of mitral disease is accentuation of the first heart sound at the apex, which, as Cossio has shown (1943) may be delayed in relation to the onset of systole (due to the hemodynamic conditions present) and preceded by a short period of systolic vibration, which may or may not be in turn preceded by a true presystolic murmur Less important corroborative signs are accentuation of the second sound at the pulmonary area, the presence of atrial fibrillation under the age of forty years, increased prominence of the left upper border of percussion dullness or roentgen ray shadow and increased width and depth of the lung hilus shadows by roentgen ray (due to the dilatation of the pulmonary blood vessels)

A diastolic thrill limited to the apex merely accompanies a marked mitral diastolic murmur

Another strongly suggestive and practically pathognomonic sign of mitral disease is the electrocardiographic evidence of abnormal right ventricular preponderance combined with atrial fibrillation The abnormal right ventricular preponderance alone with normal rhythm and increased atrial or P waves is found also in congenital pulmonary stenosis or interatrial septal defect, but with a rheumatic history and a systolic murmur limited to the apex it strongly favors mitral valve disease the occurrence of atrial fibrillation with abnormal right ventricular preponderance is rare in congenital heart disease and common in mitral disease (Figures 128 and 129)

The blood pressure is of no importance in the diagnosis of mitral disease; it may be normal, low or high. A low systolic pressure with small pulse pressure is common but hypertension of the essential type is a not infrequent complication even in well-marked mitral stenosis.

Other signs found with mitral disease are merely those due to various complications.

Course and prognosis. The chief cause of chronic crippling of the heart in young adults is extensive mitral disease of rheumatic type lesser grades of mitral stenosis or regurgitation, or of both combined often permit long lives with relatively little crippling

The course and prognosis of mitral disease vary according to the extent of the lesion, the etiologic factors, and the complications. The lesion may be so slight that there is little or no deformity of the valve with little or no stenosis or regurgitation In such cases the course is that of a person with a normal heart, and the prognosis is excellent with but one exception which is, however important. A damaged mitral valve, whether or not discovered clinically is a liability in that it is much more frequently than is a normal valve the site of repeated rheumatic infection in youth and, if there is not much mitral stenosis, of bacterial endocarditis in youth and middle age.

If there is marked and preponderant stenosis of the mitral valve in youth the victim develops symptoms and signs of diminished cardiac reserve and frequently of atrial fibrillation (in over one half of the cases) and dies usually

of congestive failure due to right ventricular exhaustion in young adult life or middle age, especially in the presence of a recurrent rheumatic infection or pulmonary infarction. The high pressure in the pulmonary circulation occasionally results in bleeding, slight as shown by bloodstained sputum, or extensive with hemoptysis. Occasionally complications, like pericarditis or cerebral embolism from intra-atrial thrombosis in the cases with atrial fibrillation, hasten death. The duration of life after the establishment of well-marked mitral stenosis averages ten to twenty years, but occasional cases far exceed this length of time while other cases die within a few months to a year or

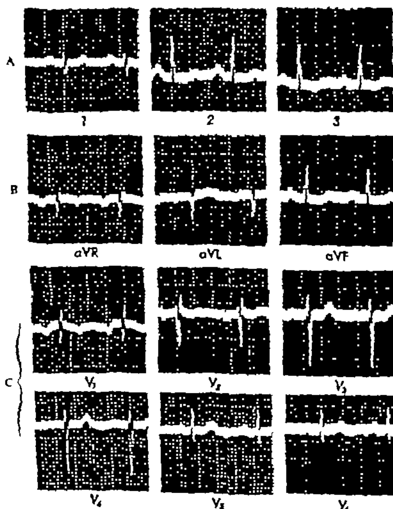


FIG. 128 Electrocardiogram in a case of mitral stenosis showing normal rhythm, female, age 43. (*A*) Bipolar limb leads 1 2, and 3 (*B*) unipolar limb leads, aVR, aVL, and VF (C) six precordial leads, V to V inclusive. Note right axis deviation in limb leads and wide *P* waves. Time = 0.04 and 0.20 second; amplitude 1 mm = 0.10 mv

two In the last edition of this book I noted that four cases of moderate degrees of "rheumatic" mitral stenosis exceeding the age of 80 years and proved at autopsy had come to my notice (White and Bland, 1941) In one of the four namely Dr Herman F Vickery there had never been any cardiac symptoms during a very active life until angina pectoris on effort, due largely or wholly to coronary heart disease, developed at the age of 77 years. At autopsy after death from pneumonia in his eighty-fourth year the heart was

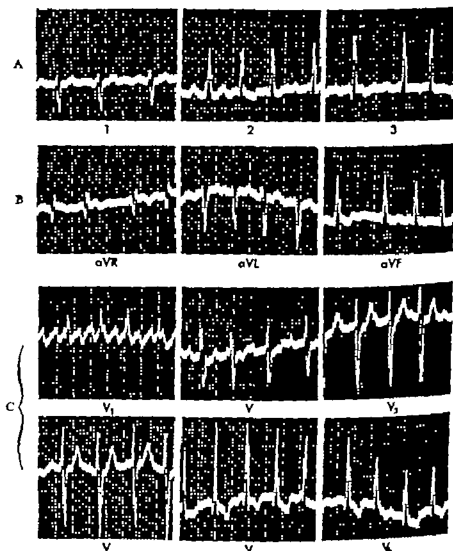


FIG. 129 Electrocardiogram in case of mitral stenosis showing coarse atrial fibrillation and right axis deviation female, age 14 (A) Bipolar limb leads 1, 2, and 3 (B) unipolar limb leads, aVR, aVL, and aVF (C) six precordial leads, V to V inclusive. Note also the regular rapid atrial action (450 per minute) resembling flutter in Lead V Time = 0.04 and 0.20 second, amplitude 1 mm = 0.10 mv

but slightly heavier than normal and the left atrium was very little, if at all, enlarged (the heart rhythm had been normal) Since 1941 I have encountered several more very old persons with rheumatic mitral stenosis.

Marked mitral regurgitation is a greater strain on the heart than is mitral stenosis and life is shorter usually lasting but a few years at best. It should be emphasized again that the degree of mitral regurgitation is indicated roughly by the intensity of the apical systolic murmur in that the murmur is loudest, other things being equal, when the regurgitation is moderate, and faintest when the regurgitation is only very slight or else of extreme degree, as discussed in Chapter 5 If the mitral ostium remains wide open during systole there should be no mitral systolic murmur at all, such a possibility is, however remote.

Complications. The commonest complications of mitral disease have already been mentioned. (1) pulmonary congestion without heart failure, (2) right ventricular failure, (3) atrial fibrillation, and (4) pulmonary embolism with infarction. Pulmonary congestion is especially common, and slight bleeding from this, or very rarely brisk hemoptysis from rupture of a larger pulmonary blood vessel (pulmonary apoplexy) may occur Sudden flooding of the pulmonary circulation in mitral stenosis by overactivity of the strong right ventricle due to tachycardia, from effort or excitement or paroxysmally occasionally precipitates a paroxysm of dyspnea which may or may not be asthmatic (one type of cardiac asthma—McGinn and White, 1934)

However *it is very important not to confuse this picture of pulmonary congestion with that of pulmonary embolism with infarction which is also a common complication of mitral stenosis and one often disregarded or overlooked* (Levine and White, 1937) an unrecognized venous thrombosis especially in the leg of a patient with mitral stenosis and congestive failure is more often responsible for such pulmonary embolism than is an intracardiac thrombus in the right heart chambers and is, of course, more amenable to treatment (by ligation) The thrombosis may be concealed in a leg already swollen in congestive heart failure and the pulmonary infarction may be concealed by congestive rales or hydrothorax in such a case, but unexplained fever leukocytosis, tachycardia, and sometimes hemoptysis and jaundice are clues calling attention to this complication.

Congestion of the liver due to stasis in the right heart chambers and inferior vena cava with particular effect on the low pressure in the hepatic veins is frequent. After years of such hepatic congestion, liver atrophy is found along with areas of regeneration, and finally a real cirrhosis may develop with ascites out of proportion to the degree of dependent edema. Intra-atrial thrombosis, rarely of the ball type loose in the atrium, sometimes occurs in mitral disease (more often in the cases showing atrial fibrillation) pieces of such thrombi may be thrown off to brain, kidneys, spleen, or extremities as aseptic emboli. A ball thrombus may rarely block the circulation completely but transiently with evidence of such obstruction in the peripheral circulation (absent pulses, cadaveric discoloration of fingers and toes) and brain. Marked

enlargement of the heart chambers, especially of the left atrium, may cause pressure symptoms and signs in the thorax, such as cough and very rarely recurrent laryngeal nerve paralysis (produced probably by pressure from the pulmonary artery pushed up against the aortic arch by the enlarged left atrium) Recurrent rheumatic infection is common in the younger cases and subacute bacterial endocarditis is an occasional fatal complication. Apparently valvular stenosis protects somewhat against Streptococcus viridans endocarditis, probably through failure of the valve to close in systole, there no longer being the factor of trauma at the valve line of closure to favor the lodgment of the bacteria. Angina pectoris rarely complicates mitral stenosis (see comment under Symptoms)

Rupture of the mitral valve may occur when inflamed or from trauma and rupture of the chordae tendineae which may lead to serious mitral regurgitation and congestive heart failure (Bailey and Hickam, 1944)

Other types of heart disease, thyroid, hypertensive, and coronary are at times associated with mitral valve disease syphilitic aortitis is rarely a complication. Other valve lesions are often found with mitral valve disease, especially those of the aortic valve. A variable degree of tricuspid valve disease is found in about one quarter of all cases of mitral valve involvement· percentages of 15 up to 40 have been reported. An interesting complication of mitral stenosis is congenital deficiency of the atrial septum discussed in Chapter 13 the septal defect diverts blood into the right atrium, probably almost doubling the load on the pulmonary circulation and resulting in much greater enlargement of the right heart chambers than of left.

Neurocirculatory asthenia and cardiac neurosis frequently complicate mitral disease, the latter particularly as the result of exaggeration of the importance of heart murmurs by the physician. Various other illnesses and infections, and diseases of other organs may occur but tuberculosis of the lungs is infrequently found in the presence of marked mitral stenosis.

Treatment. In the last edition of this book (1944) I stated that there was no specific therapy for mitral valve disease, that complications must be treated as such, and that the life of a person with mitral disease should be somewhat protected, especially against heart failure and against infection of rheumatic and subacute bacterial nature, but during the last few years progress has been made in two directions both surgical. An ingenious and successful anastomosis between one of the right pulmonary veins and the vena azygos has been carried out in several cases of "tight mitral stenosis" to prevent recurrent attacks of severe acute pulmonary edema through the establishment of a safety valve (Bland and Sweet, 1949) an atrial septal defect has been produced for the same purpose (Harken, Ellis, et al., 1948) The other procedure has been the evolution of more promising plastic surgery on the deformed valve itself (Bailey et al., 1949 Harken, 1950· and others) than the pioneer efforts of Cutler which had to be abandoned because of a very high mortality over twenty years ago (Cutler and Beck, 1929) The best technic now (early in 1951) is the incision or rupture of the cusp adhesions at the

commissures. The next decade may be a crucial one of further progress in valvular surgery but of far greater importance, of course, will be efforts, also beginning to look promising, to control the chief cause of valvular deformity namely rheumatic fever itself

Differential diagnosis. Mitral valve disease must be primarily differentiated from functional mitral regurgitation, from respiratory systolic murmurs, from relative mitral stenosis in cases of left ventricular dilatation with or without aortic regurgitation, from transmitted murmurs of aortic stenosis, of tricuspid stenosis, and of congenital defects (pulmonary stenosis and interventricular septal defects) and from the overactive heart in thyrotoxicosis or neurocirculatory asthenia. The signs whereby this differentiation may be made have already been discussed here I would simply reiterate that with considerable cardiac enlargement it is sometimes impossible to distinguish by clinical examination mitral valvular disease from the manifestations of left ventricular dilatation. Finally it should be said that occasionally mitral disease, even of extensive degree, may exist without proof of its existence, especially when the heart action is weak, the heart very large, or some overshadowing complication present.

B. AORTIC VALVE DISEASE

Aortic valve disease is generally considered to be more serious than mitral valve disease. The chief reason for this is that aortic valve disease is often caused by a neglected syphilitic infection. Moreover slight degrees of involvement are frequently missed in diagnosis, the soft aortic diastolic murmur being unheard and the systolic murmur of slight aortic stenosis, unattended by a thrill, being disregarded because of the absence of all other signs. As a matter of fact, disease of the aortic valve is often of very slight degree, and when it results from a rheumatic infection in youth it may be compatible with a long and fully active life.

Etiology *Cause* The cause of aortic valve disease is commonly either rheumatic or syphilitic, the former occurring more often in such parts of the world as New England where the rheumatic infection is common and the latter more often in regions where syphilis is more frequent and rheumatism relatively infrequent. Other causes of aortic valve disease are relatively rare and consist of bacterial endocarditis, collagen diseases, and sclerosis. The valve ring itself may be stretched with or without any lesion of the valve cusps this fact explains the aortic regurgitation in certain cases of syphilitic aortitis or of chronic hypertension, especially when aortitis and hypertension are combined, and in rare cases of severe anemia in a series of 200 consecutive autopsied cases of hypertensive heart disease with normal aortic valves, an aortic diastolic murmur had been found in 14 i.e. 7 per cent (Garvin, 1940) Trauma is a very uncommon cause of aortic valve lesions It occurs particularly in the case of a valve already damaged. Congenital aortic valve defects are infrequently found, the bicuspid valve is the commonest.

Age The age at which aortic valve disease is present extends from ear childhood to extreme old age. It is commonest in middle age when the rheumatic aortic valve lesion is still encountered, the syphilitic lesion most frequent, and the sclerotic type beginning to appear

Sex The male sex shows much more aortic valve disease than does the female sex, in about the ratio of 3 to 1 This is due not only to the fact that syphilitic aortitis is much more common in the male but also to the fact that the rheumatic infection involves the aortic valve more often in the male, and that sclerotic changes are also more common in that sex.

Pathology The pathology of aortic valve disease depends on the etiologic factor Active inflammation of the valve has already been discussed at the beginning of this chapter and in Chapters 14 15 and 16 It remains to discuss the chronic deformities of the valve and their effect on the heart and aorta

(a) A single mild *rheumatic* valvulitis may leave no deformity but severe or repeated infections tend to cripple the valve through adhesion of the cusps at their commissures, thereby producing stenosis of various degrees, or through scarring, retraction, and stiffening of the free borders of the cusps, thereby producing regurgitation. As in the case of the mitral valve, so here too, the rheumatic lesion usually causes both stenosis and regurgitation, giving rise rarely to regurgitation alone, except in the earliest stages, and also rarely to stenosis alone. There are varying ratios of stenosis and of regurgitation in different cases and during the evolution of a single case The end result of a rheumatic lesion or of repeated rheumatic lesions may be either preponderant aortic stenosis (Figure 130) preponderant aortic regurgitation, or equal grades of both from the clinical standpoint it is useful to attempt to make this differentiation. Preponderant regurgitation is much more common than preponderant stenosis, in the ratio of about 5 to 1 but in New England pure aortic regurgitation as determined at postmortem examination is less common than the combination of aortic stenosis and regurgitation. In Cabot's series (1926) there were 93 cases showing stenosis and regurgitation of the aortic valve and 55 cases showing regurgitation with little or no stenosis, which gives a proportion of 148 instances of aortic regurgitation to 93 of aortic stenosis. The healed rheumatic aortic valve may become calcified and stony especially when there is marked stenosis.

(b) In *subacute and acute bacterial endocarditis* the vegetations may be so large that they cause actual stenosis, or increase it if stenosis is already present, they may even project upward from the cusps and block the mouths of the coronary arteries. There may be extensive ulceration of the valve cusps with rupture or the development of small aneurysms of the sinuses of Valsalva. Usually bacterial endocarditis is superimposed on an aortic valve previously damaged by rheumatic infection, or on a congenitally abnormal valve (bicuspid especially) but it may attack a normal valve, and in its early stages, as in the case of the rheumatic lesion, there may be no deformity. Permanent deformity may result, consisting of stenosis, regurgitation, or both, with a tendency to calcification of the damaged valve.

(c) As the result of *syphilitic* involvement the commissures of the aortic valve become permanently widened to cause regurgitation (Figure 131). The aortic valve ring also may be dilated with the development of extensive regurgitation. Aortic stenosis is not the result of syphilis itself, although rarely in healed cases, complicating calcification or subacute bacterial endocarditis may cause some degree of stenosis.

(d) The *sclerotic* lesion of the aortic valve found as a primary condition in older individuals (Mönckeberg, 1904) is not commonly of a degree sufficient to cause much deformity of the valve. It is a different process from that of secondary calcification of rheumatic or other types of infectious endocarditis, although they may exist together. The sclerotic lesion is a subendocardial process beginning as atheroma and progressing to calcification, especially at the base of the valve; as it increases it grows into the valve cusps stiffening and deforming them, first at their bases, and producing a slight aortic stenosis. This kind of aortic stenosis probably accounts for an aortic systolic murmur in some elderly individuals in whom there is no evidence of aortic dilatation; a diagnosis of aortic dilatation has at times been made unjustifiably to explain an aortic systolic murmur of obscure origin. When the whole valve is involved and a stony mass projects into the aortic lumen

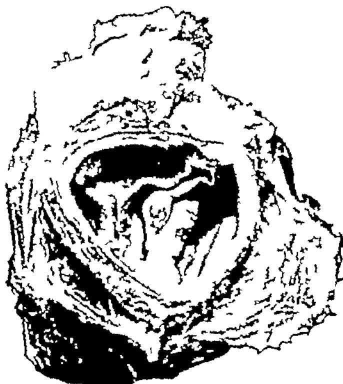


FIG. 130. Photograph showing marked aortic stenosis. Bicuspid valve. (Kindness of Dr. Ronald Grant, Guy's Hospital, London.)

resulting in well-marked aortic stenosis, Mönckeberg's sclerosis alone usually is not to blame, but rather a combination of an old infectious process and superimposed calcification. In a series of 40 cases of calcific sclerosis of the aortic valve studied microscopically with care, only 3 cases were thought to fit pure Mönckeberg's sclerosis; of the remaining 37, 18 were clearly rheumatic in origin and another 19 probably so (Karsner and Koletski, 1940). The endocardium may be eroded just as the endothelium in the aorta is at times eroded over calcified plaques.

(e) Serious *congenital* aortic valve lesions, stenosis and atresia, are very rare, but congenital bicuspid aortic valves are found occasionally and are likely to be the site of subacute bacterial endocarditis; quadricuspid aortic



FIG. 131. Syphilitic aortitis and aortic insufficiency. The aortic valves are thickened and rolled at their margins and widely separated at the commissures. The coronary mouths are obliterated. Note wrinkling and stellate scarring of aortic intima. The left ventricle is dilated and the trabeculae carneae flattened—evidence of aortic regurgitation. (W. G. MacCallum, *A Text Book of Pathology*, 1928, Kindness of W. B. Saunders Company, Philadelphia.)

valves are seldom encountered. Subaortic stenosis involving the infundibulum (outflow tract) of the left ventricle is more often found as a congenital defect than stenosis of the valve itself, but both are rare.

(f) *Rupture.* Blows and, very rarely indirect strain may cause linear ruptures of the aortic cusps at their bases or through their structure any where, even when no disease is present, probably due to a high pressure effect at the moment of valve closure associated with inferiority of tissue strength. Almost invariably however lesions due to acute or subacute bacterial endocarditis, or to syphilis, are the cause of weakening of the valve before rupture takes place. When there is some such disease present, no definite trauma is needed to cause rupture, ordinary cardiac action being sufficient.

Normally in the adult the aortic valve ring circumference measures 7 to 8 cm If it measures 5 cm or less the stenosis is marked enough to be of considerable clinical importance and should be clinically diagnosable.

Effect of aortic valve disease on the heart. The effect of aortic valve disease on the heart itself is very variable. There may be no evident effect when there is no valve deformity or when there is very slight regurgitation or stenosis. Marked *aortic regurgitation* has a more rapidly serious effect than has marked aortic stenosis. The heart becomes very large with the apparently simultaneous development of left ventricular hypertrophy and compensatory dilatation, producing eventually the cor bovinum, the ox heart, which may weigh as much as 1 000 gm or more and which is, as a rule, widely dilated. The heart of "pure aortic regurgitation is on the average the heaviest and largest known. It is most often seen in syphilitic aortitis but occasionally it results from the rheumatic infection. When the left ventricular dilatation in aortic regurgitation reaches a certain degree, the mitral valve no longer remains competent and left atrial enlargement (dilatation and hypertrophy) ensues, followed in turn by right ventricular enlargement and eventually by right atrial enlargement, too, though death due to left ventricular failure is likely to interrupt the full evolution of these various steps. Pulmonary congestion occurs after the left ventricle has begun to fail.

The heart muscle may be unaffected in cases of marked aortic regurgitation other than to show great hypertrophy and to be stretched around a widely dilated left ventricular cavity with flattened trabeculae. This strong and seemingly healthy muscle may fail under the strain of the overwork which is caused by the valve lesion, abetted by defective coronary circulation which in turn is the result of the low diastolic blood pressure. Normally it is a sufficient blood pressure in diastole that maintains the coronary circulation at a proper level. Although narrowing of the coronary artery mouths by the aortitis so often accompanying aortic regurgitation may still further weaken the myocardium, actual pathologic changes in the myocardium are only infrequently seen when such changes do occur they result from concurrent occlusion or much sclerotic narrowing of the coronary arteries, or from rheumatic myocarditis if there is an active rheumatic infection.

Marked *aortic stenosis* generally of gradual development, causes steadily

increasing hypertrophy of the left ventricle with little or no dilatation until the heart begins to fail. The hypertrophy is of the "concentric" type as compared with the "eccentric" type in aortic regurgitation, and the heart remains relatively small in bulk although considerably increased in weight. Eventually the heart in aortic stenosis may become two or three times the normal weight, but this occurs much more readily if considerable aortic regurgitation is also present. The other heart chambers are unaffected in aortic stenosis until the left ventricle fails. It is surprising to discover how well aortic stenosis may be borne, even by old persons, and yet it must be considered a constant strain on the left ventricle and a possible cause of sudden death. Congenital subaortic stenosis acts on the heart much as does acquired aortic stenosis itself.

Effect of aortic valve disease on the aorta. Aortic dilatation is commonly found with marked aortic regurgitation, especially when the aorta is the seat of a syphilitic process with loss of its elasticity and muscular control; even with rheumatic aortic regurgitation the aorta becomes somewhat stretched, but not so much permanently as temporarily with each systole. In cases of preponderant aortic stenosis the aorta may be normal in caliber and in other respects also

Symptoms. The only symptoms of aortic valve disease itself are a tendency to faintness, dizziness, or even syncope in patients with marked aortic stenosis and to throbbing, forceful pulsation of heart and arteries in patients with marked aortic regurgitation. In advanced cases it is common to find symptoms of left ventricular failure, such as paroxysmal dyspnea with or without cardiac asthma, and of coronary insufficiency (angina pectoris) without other cause than the aortic valve disease In some young individuals, usually of nervous type, aortic regurgitation, especially when marked in degree, is attended by paroxysmal angina pectoris and hypertension even at rest.

Signs. The early stage of acute rheumatic aortic valve involvement and even the chronic aortic valve lesion, too, may be so slight in degree that there is no valve deformity and therefore no sign of disease of the valve. The same is true of acute bacterial endocarditis, of syphilitic invasion, and of sclerotic change in their earliest stages, but when the valve is deformed there are always signs of its affection, except in moribund conditions. The clinical proof of aortic valve disease rests primarily on auscultatory findings.

Aortic stenosis when very slight, is without signs or attended by only a minimal systolic murmur when of moderate degree it is accompanied by a loud systolic murmur in the second intercostal space just to the right of the sternum with or without a slight palpable thrill and with slight to moderate cardiac enlargement of the left ventricular type. When the stenosis is of considerable degree the aortic systolic murmur is very harsh and widely transmitted especially along the great vessels toward neck and arms and even into the abdominal aorta, the aortic systolic thrill is marked, the second aortic sound is often absent, the heart is considerably enlarged, and the peripheral pulse is small and often of plateau or anacrotic type with low systolic and small pulse pressure (see Chapter 8)

The triad of murmur thrill, and small pulse is the essential finding; the other findings are corroborative. It is not necessary however to wait for an aortic systolic thrill or a plateau pulse to make a diagnosis of aortic stenosis the diagnosis can be made on the aortic systolic murmur alone in a patient without aortic dilatation or hypertension, provided the murmur is loud and harsh. Accuracy of diagnosis has increased greatly in our hands since we have made this change in the diagnostic criteria of aortic stenosis. It is, furthermore, of great interest to remember that the systolic murmur of aortic stenosis is well transmitted to the cardiac apex but not to the lung bases in back, while the systolic murmur of mitral regurgitation is well transmitted to the lung bases in back but not to the base of the heart. The heart rhythm is usually normal in aortic stenosis.

There is a characteristic roentgen ray picture of the heart somewhat enlarged by the presence of relatively uncomplicated aortic stenosis (without hypertension or myocardial failure and with little or no aortic regurgitation) there is a compact concentric enlargement of the left ventricle without increase of pulmonary artery and with little aortic prominence (Figure 132) The electrocardiogram in time develops the pattern of left ventricular enlargement (high *R* waves and depressed or inverted *T* waves in Lead 1 and in the precordial leads over the left ventricle, V_4, V_5, and V_6) (Figure 133 page 691) as in the case of the hypertensive heart (see Figure 97 page 477)

The signs of congenital subaortic stenosis are essentially the same as those of acquired aortic stenosis.

Aortic regurgitation is shown by the presence of an early blowing diastolic murmur heard maximally along the left sternal border over the sternum itself at the level of the second and third ribs, or in the second intercostal space just to the right of the sternum, provided one can rule out pulmonary regurgitation, which is a very rare valve defect. Pulmonary regurgitation can almost invariably be excluded by the absence of marked mitral stenosis (which is the usual factor behind pulmonary regurgitation) and by the absence of the very rare congenital or acquired pulmonary valve disease with regurgitation.

The heart may not be found appreciably enlarged on either physical or roentgenologic examination in the presence of a slight degree of aortic regurgitation which is sufficient nevertheless to give a characteristic murmur nor need there be in such cases any abnormality of blood pressure or of the character of the peripheral pulse. Cardiac enlargement, particularly of left ventricular type is readily found by any method of study in the presence of considerable aortic regurgitation, associated with such enlargement are a full pulse pressure due to a low diastolic pressure (often as low as 30 or 40 mm of mercury and sometimes not measurable above zero) a water-hammer pulse, capillary pulse, in very rare cases even pulsation of the spleen, a double murmur in the great arteries when compressed (Duroziez's sign, Duroziez, 1861) and a double murmur at the base of the heart. The roentgen ray in such cases, besides showing the left ventricular enlargement (Figure 132)





FIG. 132. Roentgenograms of the thorax in two cases of aortic valve disease: (*A*) stenosis, (*B*) regurgitation. Both young men. (Kindness of Dr Hugo Roesler Temple University Philadelphia.)

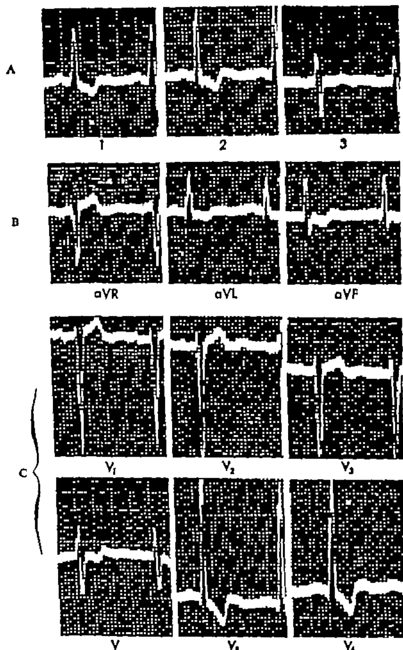


FIG. 133 Electrocardiogram I case of aortic stenosis with enlargement of the left ventricle, female, age 59 (*A*) Bipolar limb leads 1 2, and 3 (*B*) unipolar limb leads, VR, VL, and VF; (*C*) six precordial leads, V to V inclusive. Note especially the deep *S* waves in Leads V to V inclusive, and the high *R* waves and inverted *T* waves in Leads 1 ., V and V_6. Time = 0.04 and 0.20 second amplitude 1 mm = 0.10 m

usually reveals a full ventricular pulse with increased pulsation in the aorta. The electrocardiogram usually shows abnormal left ventricular preponderance with high *R* waves and inversion of the *T* waves in Leads 1 V_4, V_5, and V_6 in these marked cases very similar to the record in marked aortic stenosis (see Figure 133 page 691) If we wait, however for all the confirmatory signs of marked aortic regurgitation before making the diagnosis, we shall miss about half of the cases, namely those in which the lesion is too slight to give more than the characteristic murmur and perhaps a little cardiac enlargement.

A combination of aortic stenosis and aortic regurgitation gives signs midway between the extreme signs of the individual defects.

Course and prognosis. Slight grades of aortic valve disease of rheumatic origin appearing in youth and sometimes discovered accidentally on routine examination are often well supported without symptoms during long and active lives. Such lesions are however always a menace because of the possibility of recurrent rheumatic infection with more definite crippling, or of bacterial endocarditis superimposed on the valve already damaged. Marked aortic regurgitation is always a serious burden, and if it is of syphilitic origin it may not permit more than a few years of life. Although marked aortic stenosis is also an important burden, it is a lighter one than marked aortic regurgitation, in part because an *active syphilitic process is not a factor* In some cases it may limit the duration and activity of life relatively little and I have found the gradual development of aortic stenosis over a period of years a good omen in a young adult who starts off with a considerable degree of rheumatic aortic regurgitation. However in either case, regurgitation or stenosis, the less the physical strain or frequency of infection, the longer the life. Congestive heart failure and angina pectoris are frequent causes of death in aortic valve disease. Also unexplained syncope and sudden death are not rare in aortic stenosis of high degree. Sudden death in aortic stenosis was first recorded by Bonetus in 1679 (see below) it occurred in 18 per cent of 100 cases of calcareous aortic stenosis analyzed by Horan and Barnes (1948) When congestive failure first appears in either aortic stenosis or aortic regurgitation it is difficult to control, recurs quickly and indicates usually a short survival of a few months to a year or two

Bonet, T *Sepulchretum, sive Anatomia Practica*. Leonard Chouët, Geneva, 1679. Vol. I, Book II, Section XI (De morte repentina, on sudden death) Observation XXVI. (Translation my own.)

"*Anatomy of a man who died suddenly and whose semilunar valves situated at the mouth of the aorta were turned to bone*

A Parisian tailor residing in the district of St. James, full-blooded and inclined to obesity and not yet old, having dined and left his house had walked hardly 40 paces when he suddenly fell to the ground and expired.

"Carried back to his home his body was opened, and no disease was found anywhere except that the three semilunar cusps, situated at the entrance of the aorta from the left ventricle were discovered to be bony I received one of these as a

gift and found it of whitish color and so hard that it could hardly be incised with a knife."

Complications. Aside from the complications of mitral valve disease, congestive failure, angina pectoris, and subacute bacterial endocarditis in aortic valve disease, other direct associations are rare. For instance, atrial fibrillation is infrequent, and hypertension is not very common. Coronary disease of high degree is, however, sometimes found, as is also neurocirculatory asthenia, and it is important to note that the blood pressure may be quite high even in the presence of marked aortic stenosis.

Treatment. There is as yet (1950) no adequate reparative treatment for aortic valve disease itself, although much promising research is in progress, with respect both to plastic surgery and to artificial valves.* However, the etiologic factors—syphilis and rheumatism—should be treated if they are still active. Congestive failure and angina pectoris should receive therapy as such without regard to the valvular disease.

The discovery of aortic valve disease even of slight extent demands some consideration. It should neither be exaggerated nor underrated. The individual should not be made into a neurotic cripple; on the other hand, he should be given an intelligent explanation of his trouble and advised to protect himself against strenuous exertion or fatigue. Foci of infection should be eradicated and respiratory infections should particularly be avoided. Penicillin should be administered at the time of dental extractions to give protection against subacute bacterial endocarditis.

Differential diagnosis. Aortic valve disease must be differentiated from functional aortic regurgitation, pulmonary regurgitation, pulmonary stenosis, patent ductus arteriosus, interventricular septal defect, aortic dilatation or aneurysm, a venous hum in the neck transmitted to upper chest, and marked peripheral vasodilatation. The differentiation is generally easy; the commonest errors are in confusing dilatation of the aorta with aortic stenosis and in overlooking slight aortic regurgitation. The discussion above of the signs in aortic valve disease covers the differential points. *It may be impossible to distinguish* aortic regurgitation due to valvular disease from that of functional type; the latter is so much less common, however, that it is generally safest to disregard the possibility of its occurrence in an individual case except in severe anemia or in a case of chronic hypertension with variable aortic diastolic murmur. As a rule when functional aortic regurgitation is diagnosed clinically, it is found at postmortem examination that aortic valve disease is present. The greatest problem of all lies in the differential diagnosis of etiologic factors behind aortic regurgitation; sometimes this problem is insoluble during life despite careful study, and even postmortem examination may fail to give the answer.

C. TRICUSPID VALVE DISEASE

Tricuspid valve disease has been of very little clinical importance as compared with disease of the mitral, aortic, and even of the pulmonary valves.

* Most recently (autumn 1951) surgical approach to the problem by dilatation of the stenosed aortic valve is being explored by Bailey of Philadelphia.

The reasons for this are three. In the first place, deformity of the valve sufficient to be of clinical significance is rare. Secondly when such deformity is present it is usually overshadowed by a higher and much more important degree of mitral valve disease. And thirdly except in rare instances tricuspid valve disease has not been diagnosed ante mortem though it has been sometimes suspected. Recently however there has been an improvement in the accuracy of diagnosis, as witness a 34 per cent correct diagnosis in fifty cases of tricuspid stenosis found among 150 patients with rheumatic heart disease studied post mortem (Aceves and Carral, 1947)

Tricuspid valve disease rarely occurs without other valve lesions. In a series of 173 cases (Osler and Gibson, 1915 including for the most part cases originally collected by Leudet, 1888) tricuspid stenosis is said to have been found alone in only 12, and in all these 12 the lesion was apparently of congenital origin in 158 there was also a mitral lesion, further complicated by an aortic valve lesion in 58 and by a pulmonary valve lesion in 3 in 3 cases the tricuspid and pulmonary valves were involved. None of the 30 cases of tricuspid stenosis personally observed by Dressler and Fischer (1929) were uncomplicated by mitral valve disease In another study 39 per cent of cases with both mitral and aortic valve disease had also tricuspid stenosis of some degree (Eimel, Fell, and Stone, 1931) A later analysis by Cooke and White (1941) has shown affection of the tricuspid valve in 47 (22 per cent) of 217 cases of rheumatic heart disease among 4 300 autopsies at the Massachusetts General Hospital between 1920 and 1937 but in only 30 of these (14 per cent) was tricuspid stenosis thought to be of sufficient degree to be of clinical importance. Another study by Smith and Levine (1942) revealed 32 cases of tricuspid stenosis among 340 individuals with rheumatic valvular disease in 4 437 autopsies at the Peter Bent Brigham Hospital from 1913 to 1940 inclusive.

Etiology The causes of tricuspid valve disease are exactly those of mitral disease, most commonly the "rheumatic" type of infection with verrucose endocarditis, thickening of the valve on healing with fusion of cusps, and fusion and shortening of the chordae tendineae in advanced cases. Acute and subacute bacterial endocarditis, sclerosis, and trauma are rare causes of tricuspid disease, as are also such congenital defects as displacement and insufficiency (Ebstein, 1866 Yater and Shapiro, 1937) stenosis, and atresia.

The *age* and *sex* incidences of tricuspid valve disease correspond roughly to those of mitral disease, children and young adults chiefly being affected and females slightly more often than males, although in one series of cases the sexes were evenly divided (21 to 21) and the age at death averaged very much less than that in rheumatic heart disease in general (23 years as compared with 42 years) (Cooke and White, 1941)

Pathology Pathologically in tricuspid valve disease, as in the case of the mitral valve, regurgitation and stenosis are almost invariably associated, although either one may preponderate Stenosis of clinical importance and in some cases diagnosable clinically is reached when the circumference of the adult tricuspid valve ostium, normally 11 to 13 cm (average 12 cm) is reduced

to 8 cm or less. The appearance of the stenosed tricuspid valve is much like that of the stenosed mitral valve, in fact when there is a tricuspid diaphragm with a small ostium in its center a view from above looking into both atria gives a strikingly symmetrical appearance on both sides. Functional tricuspid regurgitation is common with right ventricular dilatation associated with congestive heart failure (Figure 126, page 671) but occurs also with other factors like anemia and pulmonary regurgitation.

Effect of tricuspid valve disease on the heart Well-marked tricuspid stenosis, if uncomplicated, naturally affects little of the heart itself except the right *atrium which becomes enlarged, tricuspid regurgitation* causes enlargement of both right heart chambers. Since, however there is practically always involvement of some other valve as well as of the tricuspid, one finds a combination of effects on the heart chambers. Practically speaking, tricuspid stenosis acts wholly on the circulation as a process obstructing the return of blood to the heart comparable to the effect of chronic constrictive pericarditis, and is not a factor causing myocardial strain or failure except in very rare congenital cases.

Symptoms and signs. Tricuspid valve disease usually causes neither symptoms nor distinctive clinical signs. If it is considerable, there may be suggestive signs and rarely conclusive evidence, if not masked by complicating factors like mitral disease and heart failure.

Tricuspid stenosis of high degree may give rise to a middiastolic murmur heard maximally at the lower end of the sternum, but usually distinguishable with difficulty if at all, from the more marked mitral stenosis murmur transmitted from the apex in very rare cases the two different murmurs may be sharply localized or the tricuspid murmur may be preponderant. Other corroborative signs of tricuspid stenosis are right atrial enlargement (see Figure 120 page 651) increased jugular venous pulse (*especially a marked chronic deep systolic jugular pulse* in the absence of an irreversible tricuspid ring dilatation) liver pulsation in the absence of other evidence of congestive failure, and, fluoroscopically enlargement and pulsation of the superior vena cava and unusually clear lung fields, with a tendency of the esophagus to be deviated to the left by the enlarged right atrium (superimposed on the big left atrium which in marked mitral stenosis more often displaces the esophagus to the right) The increased systolic pulsation of neck veins, vena cava, and liver is of course due to tricuspid regurgitation, but in the absence of pure dilatation of the tricuspid ring this means tricuspid valve deformity more often in the form of a diaphragm, causing both stenosis and regurgitation. Almost invariably atrial fibrillation is present so that the jugular and liver pulses show only ventricular waves, but in very rare cases normal rhythm persists and a very large *a* wave due to the contraction of the powerful and obstructed right atrium is seen in the neck veins as a striking phenomenon (Puddu, 1951)

Tricuspid regurgitation due to valvular disease is more likely than is functional regurgitation due to heart failure to show a systolic murmur localized at the lower end of the sternum, because in the former case the strength of

the ventricular contraction is greater and the tricuspid ostium does not tend to remain so wide open during systole. In the rare cases of well-marked tricuspid regurgitation without heart failure the jugular and other venous pulses are especially pronounced with greatly exaggerated *c* or ventricular contraction waves, without the sustained stasis waves uniting the *c* and *v* waves (see Chapter 8) It is important not to confuse the deep systolic jugular pulse with vigorous carotid arterial pulsation, an error frequently made. Fluoroscopically the superior vena cava and the right atrium are seen to pulsate markedly, especially at the time of ventricular systole. Finally the liver pulse is likely to be more marked than with any other conditions it shows a great preponderance of the ventricular wave. Pulsation of the spleen also has been noted (Sutton and Rawson, 1935) But there may be neither hepatic nor splenic pulsation evident clinically in proved cases of tricuspid stenosis. Other studies such as arterial blood pressure measurement and electrocardiography are of little or no value in the diagnosis of tricuspid valve disease the electrocardiogram almost invariably shows right ventricular preponderance due to the mitral stenosis also present.

The course and prognosis, complications, and treatment of tricuspid valve disease are somewhat similar to those already noted in the discussion of mitral valve disease and in fact are almost invariably dependent on them, since the mitral lesion is usually greater in degree and far more important. There are, however two qualifications necessary in the first place, the presence of tricuspid valve disease of importance signifies a higher degree of heart disease than when mitral, or mitral and aortic, valve disease is present without tricuspid valve deformity and so death comes considerably earlier (averaging in Cooke and White s series only 23 years in contrast to 42 years for all the rheumatic heart cases) and, in the second place, after systemic venous congestion has set in life lasts longer in the cases with tricuspid stenosis than in those without, due to the protection of the heart and lungs by the mechanical obstruction of the stenosed valve from engorgement with blood. Thus, well-marked tricuspid stenosis acts much as does chronic constrictive pericarditis in causing an invalid or semi-invalid life for years with little dyspnea but with big liver and ascites, often requiring paracentesis or diuretics, in contrast to the much shorter life of the patient with pure mitral stenosis after congestive failure has once set in. However there is no advantage at all in this, for not only does the tricuspid patient have a longer spell of congestion but he lives a considerably shorter life than does the mitral case. The younger tricuspid patients who die succumb as a rule as do the younger mitral ones, to the myocardial effects of recurrent active rheumatism Surgical repair of deformed tricuspid valves has not yet been attempted so far as I am aware.

The differential diagnosis of tricuspid valve disease is very difficult and has been referred to above stenosis of this valve may be indistinguishable from mitral stenosis, while organic tricuspid regurgitation may give signs that easily lead to an incorrect diagnosis of mitral regurgitation with functional tricuspid regurgitation caused by right ventricular dilatation. The rare irreversible dilata-

tion of the tricuspid ring, with little or no myocardial failure and without any tricuspid valve deformity (Fischer 1933) may be indistinguishable from tricuspid valve disease. Chronic constrictive pericarditis can be easily distinguished by the absence of any evidence of organic valvular disease in that condition.

D PULMONARY VALVE DISEASE

Congenital stenosis of the pulmonic valve or of the right ventricular out flow tract (*infundibulum*) below it, *is one of the most important and interesting* of all valvular defects. Although uncommon, it has lately held the limelight. Other pulmonary valve lesions, congenital or acquired, are very rare. The other valves are usually normal when the pulmonary valve is deformed.

Etiology The causes of pulmonary valve disease are as follows first, congenital stenosis or atresia, the former (stenosis) with or without septal defect, the latter (atresia) always with such defect, second, rheumatic infection which, though it may attack the pulmonary valve acutely very rarely leaves any deformity third, acute and subacute bacterial endocarditis.

When pulmonary regurgitation is found, it is almost always functional in character and due to greatly increased pulmonary arterial blood pressure and pulmonary artery dilatation, resulting most commonly from advanced mitral stenosis.

Pathology The usual pulmonary valve lesion of congenital nature consists of a fusion of the cusps, generally into a diaphragm with a small opening in the middle of it, a high degree of stenosis resulting. In some cases this lesion appears to be the result of a fetal endocarditis. Normally the circumference of the adult pulmonary valve should measure 8 to 9 cm it should be considered too small if it measures 6 cm or less. Rarely the cusps may be defective or absent so that regurgitation results. In some instances the base of the valve is a part of a narrow canal caused by faulty fetal development. The pulmonary artery itself may be smaller or larger than normal, or it may be of normal caliber generally it is considerably enlarged when there is pulmonary valve stenosis.

In many of the cases of so-called congenital pulmonary stenosis the pulmonary valve itself is normal or simply of small size without other deformity the stenotic lesion being located in the region of the *infundibulum* of the right ventricle 2 or 3 cm below the valve and often separated from it by a cavity of variable size. This should actually be called infundibular stenosis. In such cases there is usually an interventricular septal defect and often dextroposition of the aorta, giving rise (with right ventricular hypertrophy) to the commonest adult lesion associated with the morbus caeruleus or maladie bleue, namely the tetralogy of Fallot (see Chapter 13)

An abnormal number of cusps, two or four sometimes comes from fetal maldevelopment, and a very rare congenital defect is valvular deficiency with regurgitation resulting.

Acquired organic pulmonary regurgitation is rare and usually due to bacterial endocarditis complicating congenital heart disease· pathologically it resembles bacterial endocarditis of the aortic valve.

Aschoff bodies have been found in the pulmonary valve in active rheumatic heart disease but it is rare for the rheumatic infection to result in any actual deformity of the pulmonary valve.

The effect of pulmonary valve lesions on the heart The effect of pulmonary valve lesions is primarily on the right ventricle, causing hypertrophy and, in the case of regurgitation and of failure dilatation also. The largest right ventricle is found with congenital pulmonary stenosis, its weight often exceeding that of the left ventricle and even reaching a figure three times the normal; in such a case the cardiac apex is made up more by the right ventricle than by the left (Figure 64 page 299) The myocardium strongly hypertrophied, is usually healthy but it may eventually fail under the strain of the valvular defect. The right atrium also is as a rule enlarged with pulmonary valve disease.

The effect of pulmonary valve lesions on the pulmonary artery Infundibular stenosis of congenital origin, generally a part of the tetralogy of Fallot, is accompanied by a pulmonary artery and circulation of smaller caliber than normal unless there are other congenital defects giving rise to dilatation of the artery On the other hand, pulmonary valve stenosis and pulmonary regurgitation are attended by some dilatation of the artery most marked of course in the "functional" cases when the arterial dilatation precedes the valvular deficiency

Symptoms and signs. There are no symptoms of pulmonary valve disease apart from those of associated conditions such as congenitally defective circulation, bacterial endocarditis, and heart failure. There are a few characteristic signs.

Pulmonary stenosis gives a harsh systolic murmur accompanied by a palpable thrill maximal in the second intercostal space just to the left of the sternum this murmur with thrill is diagnostic, if aortic stenosis, patent ductus arteriosus, interventricular septal defect, and aortic aneurysm can be excluded; such exclusion is usually an easy procedure. Cardiac enlargement is not marked when it involves the right ventricle, but physical examination and roentgen ray study often show an increase of dullness and shadow transversely to the left, sometimes giving the characteristic coeur en sabot shape of marked right ventricular preponderance with decreased pulmonary vascular shadows. The electrocardiogram shows the highest degree of right ventricular preponderance found in any condition, with abnormally large *P* waves due to the right atrial enlargement (Figure 73 page 320) If a congenital ventricular or atrial septal defect is also present, there is cyanosis, often of high degree, as in the tetralogy of Fallot. In the markedly cyanotic cases polycythemia and clubbing of the fingers are evident (see Chapter 13)

Pulmonary regurgitation whether due to structural valve defect or functionally produced by pulmonary hypertension and pulmonary artery dilatation, gives a blowing early diastolic murmur along the left sternal border that car-

not always be distinguished in site, time, and character from that due to aortic regurgitation, it tends to begin higher up however and often follows immediately after a greatly accentuated pulmonary second sound. The distinction between pulmonary regurgitation and aortic regurgitation must sometimes be made by other characteristics than the murmur itself, but there may be no clues in the case of very slight lesions except when the defect is functional, the big pulmonary artery and perhaps also marked mitral stenosis being evident. When the pulmonary regurgitation is pronounced, a visible pulsation is evident in the second left interspace, and vigorous pulsation of pulmonary artery right ventricle, and pulmonary hilus shadows is seen fluoroscopically The pulmonary second sound is usually increased with regurgitation if the valve cusps are not badly damaged, and it is decreased or absent with stenosis.

Course and prognosis. The course and prognosis of pulmonary valve lesions depend on the extent of the lesions. With considerable congenital stenosis and much cyanosis life is usually short, although there are rare instances on record of patients surviving to middle life or to early old age, having lived useful active lives. The lesser grades of stenosis without cyanosis are less serious. I have followed for many years a frail woman, cyanotic since early childhood, with clubbed fingers and all the signs of pulmonary valve stenosis who finally died in the year 1949 of right heart failure at the age of 75 years. She showed at postmortem examination marked pulmonary valve stenosis and an atrial septal defect. She survived 18 years longer than the oldest case with these defects previously recorded. Although the very rare cases of pulmonary regurgitation due to valvular disease are under considerable strain, they may support moderately active lives for years. Patients with functional pulmonary regurgitation do badly usually living but a few months or a year or two at best, the valve not being itself responsible for the bad prognosis as it is merely a part of the terminal stage of marked mitral stenosis or pulmonary heart disease. Death that may ensue in some cases of subacute or acute bacterial endocarditis is due not to the pulmonary valve involvement if present but to the active infection itself

Complications. The chief complications of pulmonary valve disease are right ventricular failure and subacute bacterial endocarditis. Disease of other heart valves may infrequently be associated with important lesions of the pulmonary valve rarely all four valves are involved, in rheumatic heart disease.

Treatment. In the last edition of this book (1944) I stated that there was no special treatment for pulmonary valve disease, surgical or medical, but that the victim should be protected from overexertion and infection, the underlying disease treated if possible, and complications cared for During the years that have intervened, however two surgical procedures have been introduced in treatment, the first consisting of arterial anastomosis between the aorta or its branches and a pulmonary artery to bring blood to the lungs to be oxygenated, thus by-passing the stenosed pulmonary valve ostium in cases of the morbus caeruleus, in particular the tetralogy of Fallot (Blalock and Taussig, 1945

Potts, 1946) and the second consisting of cutting the stenosed valve ite (Brock, 1948) (see Chapter 13 for details)

E. COMBINED VALVULAR DISEASE

There is no need of any particular discussion about disease of two or mo valves in the same case. The etiology pathology signs, and treatment are outlined for the individual valve lesions. The course and prognosis are nat rally more serious the more valves there are involved, provided the degree damage to the individual valves is comparable there is no exception in the ca of well-marked tricuspid stenosis which at one time was thought to impro the prognosis of other valve lesions with which it is associated, before care fully collected data corrected the error which had arisen from comparison the *duration of "congestive failure" in the cases with and without tricusp* stenosis (see above under Tricuspid Valve Disease) The commonest valv disease combinations are mitral plus aortic, and mitral plus tricuspid (se Chapter 24) In about three quarters of all cases with combined valvular di ease the mitral lesion is the essential and controlling one, and in the othe quarter the aortic valve defect requires the chief consideration.

F INTRACARDIAC THROMBOSIS

Intracardiac thrombosis is a common complication of many cardiac con ditions stasis, old scarring of the endocardium infection, and infarction; it was found post mortem in 265 or 34 4 per cent, of 771 consecutive adult autopsied patients who died of heart disease (Garvin, 1941) It is almost al ways bland, but as in bacterial endocarditis may become infected itself. It is nearly always attached to the wall of one of the heart chambers, loosely or tightly constituting a *mural thrombus* in left ventricle, left atrium, right atrium or right ventricle, or in more than one chamber free or *ball thrombi* are rare, being found in a few cases of mitral stenosis in the left atrium where they may mechanically seriously obstruct the circulation, even causing attacks of syn cope and marked feebleness of the pulse with acrocyanosis and in extreme cases purpura and gangrene of the extremities, toes, fingers, and ears. Pedun culated thrombi in the left atrium may act much like ball thrombi. A unique case of a ball thrombus in the right atrium has also been reported, it was correctly diagnosed ante mortem (Wright, et al., 1944)

The commonest cause of mural thrombi in the heart is myocardial infarc tion, fresh or old, involving almost always the left ventricle and responsible for occasional peripheral arterial embolism to eye, brain, kidney mesentery arm, or leg. Rheumatic heart disease ranks second, with thrombosis on the wall of the left atrium or in its appendage, especially in the presence of atrial fibrilla tion which so commonly complicates mitral stenosis. Bacterial endocarditis, subacute or acute is next most common as a cause of important intracardiac thrombosis, *in such cases located chiefly on the valves. Large* emboli may be ejected from the heart in either rheumatic heart disease or subacute bacterial

endocarditis. Intracardiac thrombi may be found also in coronary heart disease without infarction, hypertensive heart disease, and aortic valve disease, syphilitic or rheumatic, especially if the left ventricle and left atrium are dilated, it is rare in congenital heart disease and in the cor pulmonale. It is common for a mural thrombus to be laid down in successive layers in a cardiac, as in an aortic, aneurysm, the deeper layers slowly undergoing organization and incorporation in the endocardium itself. Anticoagulant therapy carried on for months or even years under close supervision, may be very helpful in reducing the incidence of peripheral embolism from intracardiac thrombosis.

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CHAPTER 27

PERICARDIAL DISEASE
ACUTE AND CHRONIC PERICARDITIS
WITH AND WITHOUT CONSTRICTION

Pericardial disease, which has been recognized longer than any other pathologic cardiac condition (its recognition dates back to the Middle Ages) has continued since the last edition of this book to be the subject of clinical investigations, which have led to important advances in its diagnosis and treatment.

Disease of the pericardium is a common condition, occurring less often as an isolated lesion than as a part of acute heart disease especially rheumatic carditis and cardiac infarction, or as a part of a polyserositis (with pleuritis or peritonitis) or of a systemic disease like septicemia or carcinomatosis. It may be serious in itself or merely an incident in other serious, often fatal, diseases, or it may be wholly unimportant. It is found in about 5 per cent of postmortem examinations, and is present as an acute condition in one half to two thirds of these cases. A survey made of 8,912 necropsies at the Mayo Clinic *(Smith and Willius, 1932)* showed pericarditis in 373 cases (4.2 per cent) 215 (58 per cent) of these 373 cases had acute pericardial disease, 113 with effusion and 102 fibrinous without effusion, the latter including 40 instances of "terminal pericarditis 158 (42 per cent) had *chronic pericarditis*, among which 15 cases had simply small localized patches ("milk spots" or "soldier's patches") A more recent survey of 13,353 consecutive autopsies done in the Los Angeles County Hospital during a period of seven years (1940 to 1946 inclusive) revealed 729 cases (5.4 per cent) of pericarditis; "nonspecific idiopathic pericarditis" was the most frequent type found, with rheumatic pericarditis next; tuberculous and pneumonic pericarditis were decreasing in frequency *(Griffith and Wallace, 1949)*

Disease of the pericardium is best considered under three headings, acute pericardial disease, chronic pericarditis, and congenital defects.

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The more virulent infections like pneumonia are likely to cause a purulent rather than a serous effusion.

Purulent pericarditis in which a variable amount of pus is found in the pericardial sac is a complication of disease produced elsewhere in the body by pyogenic bacteria, such as pneumococci, staphylococci, and streptococci. It may be of hematogenous origin or it may be produced by direct extension from an empyema or a mediastinal abscess. It is sometimes difficult to say whether such pericarditis is purulent or serofibrinous when the effusion is not frankly composed of pus but contains a suspension of cells which are largely polymorphonuclear leukocytes. Of a series of 300 fatal cases of pneumonia in an army base hospital, 24 per cent showed acute pericarditis, mostly of purulent nature (Stone, 1919) but this is now becoming rare due to specific therapy with penicillin and other curative agents.

Hemorrhagic pericarditis in which the exudate is largely bloody may be caused either by infection, such as tuberculosis or fulminating rheumatic fever or by malignant disease. This should be distinguished from *hemopericardium* due to hemorrhage into the pericardium, the result of rupture of aortic or heart wall or of coronary vessel caused by infarction, aneurysm, or trauma.

A rare cause of acute pericardial involvement is *malignant disease* generally metastatic but sometimes penetrating the pericardium from adjacent new growth in the mediastinum. Sarcoma and carcinoma are the commonest lesions of this sort (Figure 118 page 594) but many varieties of new growths have been found, secondary invasion of the pericardium is much more common than a primary tumor (see Chapter 23)

Still more rare is *pneumopericardium* due to the entrance of air from a pneumothorax, from esophageal or bronchial perforation, or from faulty paracentesis. Rarely air has been intentionally introduced into the pericardial sac in the treatment of tuberculous effusion.

Age Acute pericardial disease may occur at any age in accordance with the etiologic factors, it is in general most common in youth when important infections are most frequent. The majority of cases occur between the ages of 10 and 40, with an average of about 25 years.

Sex. There is a male sex preponderance in acute pericardial diseases of nearly 3 to 1 the cause for this is not clear (Cabot, 1926 Smith and Willius, 1932)

Pathology *Acute fibrinous pericarditis* consists of infiltration of the pericardium with many mononuclear and polymorphonuclear cells and a more or less adherent layer of fibrin, containing such cells, covering a part or the whole of the pericardium, starting on either the visceral or the parietal surface but as a rule eventually involving opposite surfaces. Pericarditis due to infarction is usually limited to the area of necrosis in contradistinction to the general involvement of the pericardium by infection. The exudate may be composed of a thin or a thick layer sometimes it is very massive, even a centimeter or more in thickness. It tends, especially when thick, to have an irregular uneven surface with stringy shredded masses of fibrin projecting like fur or complexly

interwoven such irregular surfaces have been termed "shaggy" or "bread and butter" pericarditis (Figure 134) A certain amount of increase of fluid in the pericardial sac (which normally contains 25 to 50 cc) is commonly found with fibrinous pericarditis. When the inflammatory or irritative process undergoes resolution and repair there may be left only a slight thickening of the pericardium local or general But when the acute process is marked in degree or extent, adhesions, partial or complete, between the visceral and parietal



FIG. 134 Photograph of heart in a boy of 12 showing acute fibrinous pericarditis in case of advanced pyelonephritis of left kidney congenital atresia of right kidney and uremia. (Kindness of Dr Benjamin Castleman, Massachusetts General Hospital, Boston.)

pericardial surfaces are common and if the inflammatory reaction has been deep, the heart may be firmly anchored to diaphragm, chest wall, pleura, or mediastinum, or it may be encased in a firm, thick, unyielding, scarred, contracted pericardium with little or no serous sac left: both of these pericardial abnormalities may coexist in the same case

It is important to note that in practically all cases of pericarditis and particularly in those with severe involvement the subjacent myocardium is also affected, it is doubtless this myocardial disease that is in the main, if not wholly responsible for the electrocardiographic abnormalities in pericarditis.

Serofibrinous pericarditis a type of pericardial effusion, begins with fibrinous pericarditis, but there is soon poured out in addition a serous exudate at varying speeds and of varying amounts from 100 up to 2,000 or 3 000 cc, the latter only if the effusion is of slow development. This extra fluid accumulates at first in the dependent parts of the sac but eventually it may distend the whole sac (Figures 135 and 136) unless it is withdrawn or subsides spontaneously If the amount is great there may develop extensive pressure on the surrounding structures—lungs, mediastinal contents, superior vena cava,

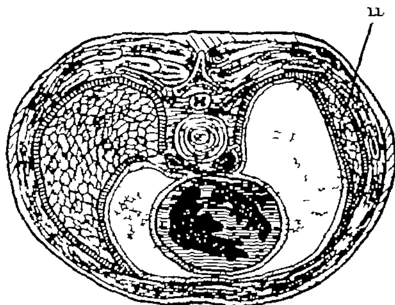


FIG. 135. Diagram of cross section of thorax showing very large pericardial effusion compressing the left lung (LL) (Conner *Am. Heart J* 1926 I, 431 Kindness of C. V Mosby Company St. Louis.)

inferior vena cava, and the mouths of the hepatic veins at the level of the diaphragm—along with dangerous pressure on the heart itself and on the great vessels within the pericardial sac (*cardiac tamponade*) Enormous effusions are sometimes seen, usually tuberculous, accumulating gradually and filling more than half the thoracic cavity In rare cases there may be a localized or pocketed pericardial effusion, sometimes in unusual locations, for example, at the right upper border of the heart where it may simulate an aortic aneurysm, such a limited effusion is the result of partial pericardial adhesions, chronic or recent, which prevent the effusion from taking the usual form.

Purulent pericarditis (pyopericardium). If the exudate either on the surface of the pericardium or in the effusion fluid contains a great majority of poly

morphonuclear leukocytes, it is called purulent· it may be thin (and watery) or thick (and creamy) and easy or difficult to aspirate.

Hemorrhagic pericarditis simply signifies a high content of red blood cor puscles in the pericardial exudate sufficient to color it red If the effusion is practically pure blood, the term *hemopericardium* is employed.

Neoplasms a rare cause of pericardial disease, may or may not induce an effusion when such an effusion occurs it is usually bloody and may contain cancer cells.



FIG. 136. Roentgenograms in case of subacute tuberculous pericarditis with effusion. (*A*) Before paracentesis; (*B*) after paracentesis; I has been injected to take the place of some of the fluid removed. Note the thickened pericardium.

Symptoms. Acute pericardial disease is generally painless but there are two important conditions which give rise to symptoms. (1) When the pleural or outer border of the diaphragmatic pericardium is involved, frequently with complicating pleurisy pain results, usually sharp intermittent or continuous, much aggravated by or indeed sometimes felt only during inspiration, and referred to precordium, left shoulder and less often to the abdomen. A large part of the pericardium, especially the visceral surface, can be inflamed without causing pain, as is usually the case with the terminal dry or fibrinous pericarditis of uremia, and with the pericardial involvement in cardiac infarction. (2) The other important condition giving rise to symptoms in pericarditis is distention of the pericardium by a moderate or large effusion, by air or by both air and fluid. With small effusions there are no symptoms with large effusions, especially those developing rapidly and with extensive hemopericardium, pressure symptoms may be extreme and a condition called cardiac tamponade or acute constrictive pericarditis results. These pressure symptoms are of two sorts those due to compression of the heart whereby insufficient blood enters the heart, the lungs, and the systemic arteries, with resulting dyspnea, weakness, faintness, venous congestion, and epigastric and right upper quadrant discomfort from hepatic engorgement; and those due to compression of lungs, trachea, bronchi, esophagus, and great vessels, with further dyspnea or orthopnea, irritative cough, hoarseness, and dysphagia. Distressing dyspnea and thoracic oppression are common symptoms of a large pericardial effusion, and the patient often assumes a characteristic attitude of distress, sitting upright and leaning forward.

Signs. The signs of acute pericardial disease, like the symptoms, are due first to the fibrinous exudate and second to the effusion. The characteristic sign of acute pericarditis often found at some stage of the disease is the *friction rub* but in many cases (over 75 per cent) it is absent or escapes notice (Cabot, 1926 a friction rub was heard in only 40 or 21 per cent, of 186 cases of acute pericarditis) It may be heard anywhere over the precordium and sometimes, when marked, even in the back or neck, but it is commonest along the left border of the sternum. It is usually rough and grating, sounding near to the ear and increased by pressure of the stethoscope, but sometimes it is so soft and gentle that it is distinguished with difficulty from heart murmurs. It is heard as a rule both in systole and in diastole, especially in the earlier parts of each but it may be almost continuous, or it may be very brief and limited to systole alone, being heard perhaps during only one phase of respiration. It may be transient, lasting but a few hours, or it may persist with little change for weeks. It is often audible even in the presence of an effusion, but sometimes it disappears or is dulled when an effusion develops. The pericardial friction rub if marked, can be felt as well as heard.

The other characteristic signs of acute pericardial disease are those produced by an effusion. An amount less than 150 cc is probably not discoverable by any method of examination since it produces no definite signs. In fact effusions of less than 300 cc are usually missed clinically The presence of a pericardial

friction rub should cause careful search for early signs of an effusion which may appear with the friction rub or shortly after it disappears. The earliest sign is roentgenologic and consists of a bulging of the lowest corners of the heart shadow because of the collection of fluid at these points it is especially well seen in the oblique views fluoroscopically As more fluid gathers it tends to fill in the hollows and grooves of the heart and great vessels, rounding out their contours and obscuring and eventually abolishing the cardiac landmarks; this change, at first apparent by roentgen ray is later found by percussion also. The "cardiac" shadow and area of dullness often rapidly increase with the accumulation of fluid, giving rise sometimes to an erroneous diagnosis of acute cardiac dilatation. The increase may be very great so that the effusion shadow and the area of dullness may extend to the left axilla (Figure 136) A characteristic change in shape of the effusion shadow occurs with change of position, the shadow in the recumbent position being globular and that in the upright position pyriform (pear-shaped) often obscurely likened to the shape of a "water bottle." This change of shape is, of course due to the effect of gravity It is sometimes of considerable value in distinguishing between pericardial effusion and marked cardiac enlargement. By fluoroscopy and teleroentgenography the heart shadow itself is almost invariably buried in the shadow of the pericardial effusion since the densities of heart and effusion are almost the same. The cardiac pulsation fluoroscopically may be much diminished or even absent. An obtuse right cardiohepatic angle of percussion dullness (Rotch s sign) is found with large effusions.

An early sign of the *cardiac tamponade* or *acute constrictive pericarditis* due to pericardial effusion is enlargement of the liver with tenderness on pressure. Slightly displaced downward, the liver is engorged, due to compression of the right atrium, great veins, and especially the mouths of the hepatic veins which open into the inferior vena cava, caused by the resting of fluid in the pericardial sac on the diaphragm at the point where the inferior vena cava comes through. Prolonged and extensive blocking of the hepatic veins may give rise to ascites with or without slight edema of the legs, which is due to coincident obstruction to the blood flow in the inferior vena cava. With very extensive effusions and the resulting compression of right atrium and both superior and inferior venae cavae, general edema may occur but this is neither common nor marked. Cyanosis of skin and mucous membranes is frequently found when the heart action is much obstructed, and the jugular veins are frequently engorged, with visible venous pulse, in the upright position.

After the development of a considerable pericardial effusion, heart sounds and murmurs are often diminished and the friction rub may disappear The blood pressure with small effusions is unchanged, but with large effusions the systolic pressure is decreased and the pulse pressure much diminished. With acute constrictive pericarditis the pulse pressure may drop to 20 cm. With very large effusions, the radial pulse may almost entirely disappear and in fact sometimes does disappear during inspiration, which is usually labored. This exaggeration of the so-called paradoxical pulse is of some diagnostic

significance (see Chapter 8) The systemic venous pressure is often greatly elevated, to 20 or 30 cm of water (normal 4 to 8 cm) Tachycardia is usual, to make up for the small cardiac output per beat, but arrhythmia is uncommon.

The one other important sign (Ewart's sign) of a large pericardial effusion is due to compression of the left lung. At the angle of the left scapula an area of variable size is frequently found over which there are dullness on percussion bronchial breathing, and increased tactile and auscultatory fremitus (Ewart, 1896) this may occasion an erroneous diagnosis of pneumonia. Recently however it has been pointed out that, in some cases at least, the Ewart's sign in pericarditis is due to an associated pulmonary lesion in the left lower lobe (infarct or "rheumatic pneumonia —Levine and Gevalt, 1940) or more likely to an accompanying pleural effusion at the left base (as a part of a polyserositis—Gordon, 1940)

Ewart described ten signs of pericardial effusion, of which the eighth and tenth are as follows

Ewart, William. "Practical Aids in the Diagnosis of Pericardial Effusion in Connection with the Question as to Surgical Treatment. *Brit. M J* 1896, I, 717

"*Eighth Sign. The Posterior Pericardial Patch of Dulness.* Whenever fluid is effused into the pericardium the normal resonance is modified at the left posterior base in a most definite way A patch of marked dulness is found at the left inner base, extending from the spine for varying distances, outwards, usually not quite so far as the scapular (angle) line, and ceasing abruptly with a vertical outer boundary Above, its extension is also variable, according to the size of the effusion, commonly it does not extent higher than the level of the ninth or tenth rib, and here again its horizontal boundary is abrupt. Its shape there is that of a square, and it is quite unlike that of any dulness arising from pleuritic effusion. You will not experience any difficulty in identifying the patch in question. Rather greater care in percussion is needed, however to follow the dulness as it extends to the corresponding vertebræ, and for a short distance also to the right of them. For some time I had overlooked this extension, which, owing to the general resonance of the right base, is one of partial dulness only When, however the effusion is considerable the extension of the patch in the right chest may become almost absolutely dull.

"I wish time permitted me to discuss with you the significance and the probable mechanism of production of this singular and most helpful sign. It is best I should confine myself on this occasion to practical points. The value of this sign is that, unlike many others, it is very sharply defined, and does not fit any other diagnosis. When, in a doubtful case, all the signs observed in front support the diagnosis of effusion, and this sign is also found, we have then in hand complete and crucial evidence of the existence of fluid, whilst when, as sometimes occurs, previous adhesion of the anterior surface of the heart to the chest wall renders diagnosis extremely difficult, this help is invaluable, and its place, so far as I am aware, cannot be supplied by any other available diagnostic method.

"*Tenth Sign. Th Posterior Pericardial Patch of Tubular Breathing and Ægophony* Immediately below or slightly to the left of the tip of the left scapula patch of about 2 inches in diameter presents well-marked tubular breathing and

ægophony This sign, although not so important as that of the patch of dullness, is very commonly if not always, present in cases of considerable effusion, and gives valuable confirmation to other signs. It has been described by other observers. The mechanism of its production is analogous to that suggested above, and is doubtless connected with pressure on the bronchi descending to that district, and with partial collapse of the pulmonary tissues. It also occurs in pleural effusions.

Other signs such as fever and leukocytosis may or may not be present, depending on the cause of the acute pericardial disease they are generally present at some time during the illness.

Electrocardiography is of distinct diagnostic value, changes in the *S-T* segments and *T* waves, and low voltage" of all complexes being frequently found with extensive acute pericarditis with or without effusion the more marked the pericarditis, the more abnormal the electrocardiogram, especially if there is a long-drawn-out course or a large effusion. The *S-T* segment and *T* wave changes in the precordial and limb leads resemble to a certain extent those found in coronary heart disease, especially those in acute occlusion over the site of infarction, namely elevation of the *S-T* segments with succeeding flattening or inversion of the *T* waves there are, however two distinct differences (1) the same *S T* segment and *T* directions are usually consistently found in all three classical limb leads in contrast to their opposite directions in Leads 1 and 3 in myocardial infarction and (2) the *QRS* waves are not affected as a rule in pericarditis as they tend to be after acute coronary occlusion. In the chest leads the *T* waves in acute pericarditis are often inverted. Sometimes the electrocardiogram returns to normal rapidly with subsidence of the acute pericarditis (Figure 137) but often some of the abnormality persists even though the patient feels well. The electrocardiographic changes in acute pericarditis have been ascribed to two factors compression of the coronary arteries by effusion or exudate, and involvement of the underlying myocardium the latter is almost certainly the more important if not the only cause. An interesting electrocardiographic distinction between massive pericardial effusion and marked cardiac enlargement has been pointed out by Tung (1941) the duration of electric systole (*Q T* interval) is normal in the former and prolonged in the latter

Paracentesis of the pericardium may prove the presence of fluid when there is an effusion, but such confirmation is unnecessary except when pus is suspected or the procedure is an essential part of treatment.

With air and fluid together in the pericardium a tinkling splash may be heard with each heartbeat.

Course and prognosis. Acute pericardial disease generally occurs either as a "benign" illness discovered on occasion in the course of a fever and clearing spontaneously without sequelae in the course of days or weeks or as a passing complication of some infection like rheumatic fever or other illness like uremia or cardiac infarction. It may not be of great importance in itself, the fibrinous or serofibrinous involvement subsiding spontaneously or occurring

simply as a terminal event in a fatal disease. Frequently the pericarditis does not even produce symptoms or signs but is discovered only at postmortem examination. There are, however three conditions in which the acute pericardial involvement is itself of great immediate importance. One is the infrequent, very serious purulent pericarditis which is usually secondary to disease else where and may be fatal unless there is ample surgical evacuation and drainage of the pus, together with specific penicillin or sulfonamide therapy and good resistance on the patient s part. The second is a pericarditis that initiates a grave miliary tuberculosis. The third is more frequent, viz., a large pericardial effusion, generally of tuberculous origin but sometimes of rheumatic or of unknown etiology which causes serious pressure symptoms and signs (acute constrictive pericarditis) and which may endanger life unless it is aspirated. But as a rule, drainage is unnecessary in acute pericardial disease.

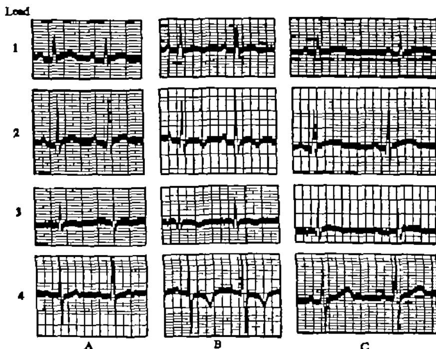


FIG. 137 Electrocardiograms (four leads) of H.C., lad of 12 years of age, at the beginning of, during, and after recovery from acute pericarditis. (*A*) Sept. 4 1942, (*B*) Sept. 8 1942, (*C*) Sept. 25 1942. Note especially the late inversion of the *T* waves in *B*

The onset of acute pericarditis is likely to be rapid but it is often masked by the underlying illness and not considered until discovered in the course of physical examination or roentgen ray study Occasionally pain calls attention to an acute pericarditis which seems to appear out of a clear sky The duration of the pericardial involvement in its acute stage varies from a few days to

a few weeks, but chronic pericarditis may result. Such chronic pericarditis may cause no trouble at all or it may produce symptoms and signs after the lapse of some months or years.

The immediate prognosis in acute pericarditis is good as a rule in the nonpyogenic and nontuberculous infections in spite of well-marked symptoms and signs, but the total mortality is still fairly high because the term "acute pericarditis" includes the terminal pericarditis of uremia and overwhelming septic infections, occasional cases of fatal cardiac infarction, and rare cases of death due to the mechanical effect of a huge or rapidly developing effusion. The introduction of penicillin and sulfonamide therapy has materially lowered the mortality in the cases with septic pericarditis during the last few years (see below under Treatment). Tuberculous pericarditis is often fatal, of one series of 24 cases of proved tuberculous pericarditis admitted to the Vanderbilt Hospital in Nashville, Tennessee, during a period of eleven years only 4 survived (Blalock and Levy 1937) and analyses of other series of cases by Keefer (1937) and by Heimann and Binder (1940) have also indicated a generally poor prognosis, although streptomycin has apparently been helpful or even curative in a few cases and it is also quite possible that cases too mild to diagnose may recover or lead to chronic constrictive pericarditis.

Hydropericardium, a part of general anasarca due to heart failure or nephritis, is not an important condition in itself the course and prognosis naturally depending on the underlying disease it does not become large enough to constrict the heart.

Complications. The acute pericardial disease is itself but a complication of infections such as rheumatic fever and tuberculosis or of other diseases like uremia and coronary thrombosis. It rarely produces complications of its own except for the establishment of pericardial effusion and adhesions. Pleuritis may follow pericarditis by contact infection though usually the reverse is the sequence Commonly associated with acute pericarditis are nephritis, valvular disease and polyserositis.

Treatment. The treatment of acute pericardial disease is wholly that of the underlying cause—rheumatic fever tuberculosis, purulent pericarditis, coronary thrombosis, or other disease—except for two conditions pain, and very large pericardial effusions.

Pain should be relieved by morphine when it is very severe for lesser grades of pain salicylates bromides, or codeine may suffice. An ice bag placed comfortably over the precordium may be received gratefully by the patient.

The pain of acute rheumatic pericarditis is often much relieved by salicylate administration, which probably also helps in the resolution of the acute process including the effusion.

For acute tuberculous pericarditis streptomycin has been tried during the past few years with benefit in some cases by injection intramuscularly (1 to 2 gm daily) and also by intrapericardial instillation, although, of course, with the risk of labyrinthitis.

If pericarditis develops in the course of a pyogenic infection or following it and is itself the cause of prolongation of the illness or of accumulation of peri-

cardial fluid, exploratory paracentesis should be done as soon as possible, or better still, to save time and the patient's strength, surgical pericardiostomy if the diagnosis of purulent pericarditis seems reasonably certain. Equally important is the administration of penicillin 300 000 units daily or the sulfonamides, e.g. sulfadiazene, 1 gm 4 to 6 times a day Cure is now possible in many such cases which in former days were rapidly fatal.

If the pus is thick it will be necessary to use a large aspirating needle or trocar sometimes only an incision will permit ready removal of the pus. The discovery of a definite purulent pericarditis demands surgical interference at once with drainage as in the case of empyema, and care should be taken that the bottom of the pericardial sac be drained. Recovery is possible in such cases if proper treatment is instituted early in the disease. If, in the development or course of a pericardial effusion, symptoms or signs (especially a rapid fall in arterial and pulse pressure and a rapid rise in venous pressure) indicate the existence of a high and perhaps dangerous intrapericardial pressure (cardiac tamponade or acute constrictive pericarditis) the pericardium should be aspirated of at least several hundred cubic centimeters of fluid, provided they are easily withdrawn without inducing disagreeable symptoms. As much as 1 000 or 1,500 cc of fluid have been aspirated in some cases. The removal of even a small percentage of a large effusion may suffice to relieve distressing orthopnea and thoracic and epigastric oppression, hypotension, and small pulse, with the saving of life and induction of convalescence.

Pericardial paracentesis may be done in several ways. It is often convenient to employ a long needle of small or average caliber (1 mm) attached to a large syringe of 50 or 100 cc capacity by rubber tubing directly or through a three-way connection which allows the fluid to be aspirated and discharged without disconnecting the syringe the direct connection is somewhat more convenient since the syringe can be easily removed and the fluid quickly ejected each time after the syringe has been filled, the rubber tube being closed by finger or clamp pressure while the syringe is disconnected. In rare cases a larger caliber needle (2 mm bore) may be necessary

The site at which the pericardium should be tapped need not be limited to one spot, for at times the fluid is more or less localized by previous adhesions, and in some cases it is more easily obtained in one place than in another Generally the best site to try first is the fifth left intercostal space 1 or 2 cm toward the sternum from the left outer border of percussion dullness and *roentgen ray shadow* and, therefore, in the case of a large effusion, usually beyond the position of the apex or left border of the heart. The skin and subcutaneous tissues should be anesthetized first, conveniently with 2 or 3 cc of 0.5 per cent procaine (Novocain) solution, using a small syringe and needle this local anesthesia, which is often omitted or is inadequately done, is wise for two reasons in the first place, for the comfort of the patient, especially since two or more attempts are sometimes necessary before the effusion is reached, and, secondly for the greater convenience of the physician who does not need to hurry or to fear a sudden movement of the patient such as may occur if sharp pain is felt. After a few minutes wait for the anesthesia to take

effect, the exploratory needle is inserted, pointed back and inward toward the spine, and forced slowly between the ribs until it is felt to penetrate the resistant pericardial membrane at a variable distance from the outer surface of the thorax, depending on the thickness of the chest wall but averaging 3 or 4 cm in the nonobese adult male When the pericardial sac is entered fluid may or may not be easily withdrawn depending on the thickness of the fluid, the caliber of the needle or trocar the position of the trocar in relation to the fluid, and whether or not obstruction of the mouth or lumen of the trocar results from a fragment of fibrin or from pressure against heart wall or pericardial surface. If no fluid comes, the needle should be variously tilted, slightly withdrawn or inserted further or completely withdrawn to be introduced again Occasionally the heart itself is felt against the trocar and may move it at every contraction this should not cause alarm for even perforation of the ventricular wall is not dangerous except in rare cases when the right ventricle or right atrium is badly traumatized or a large coronary vessel may be injured. If fluid is not found by paracentesis well out in the fifth left interspace, another trial may be made in the fourth or fifth interspace nearer the sternum, or in the fourth interspace to the right of the sternum and just inside the right border of dullness or roentgen shadow This last location is a favorable one when the effusion projects unusually far to the right. I have aspirated 600 cc of fluid from this site when adhesions prevented fluid accumulation to the left.

There are two other sites for pericardial paracentesis that have been tried and sometimes found favorable the epigastrium and the left side of the posterior thoracic wall. The epigastric site is advantageous because it drains the lower part of the pericardial sac, but special anatomic knowledge and experience are necessary so that the needle will be directed upward at the proper angle as well as backward and inward. In this method the needle is inserted high up in the sharp angle between the ensiform cartilage and the left costal border and is pointed upward at an angle of about 30 to 40 degrees to avoid peritoneum and diaphragm the pericardial sac being encountered at a depth of about 3 or 4 cm. The left posterior thoracic site is useful in rare cases in which fluid is not obtained by paracentesis in the usual positions but is almost certainly present as indicated by pulmonary pressure signs at the angle of the left scapula (Ewart s sign) provided one can rule out pulmonary consolidation or pleural effusion as a cause of the "Ewart s sign, not always easy to do. With the left arm of the patient raised to move the scapula outward the needle is inserted, after local anesthetization in the seventh or eighth intercostal space in the midscapular line. Insertion to the depth of 5 to 8 cm should yield fluid from a distended pericardial sac. I have withdrawn 500 cc of pericardial fluid through the back, affording great relief to the patient, when attempts through the anterior chest wall were unsuccessful and the need of pericardial paracentesis was urgent. There is no danger of pleural or lung infection by this procedure unless purulent pericarditis is present, in which case this site for the paracentesis should of course be avoided.

Aspiration of the pericardium usually does not have to be repeated, either

the serous effusion soon subsides, or operation, with drainage, is carried out for purulent pericarditis. In a few cases, however especially those of tuberculous origin, it may be necessary to aspirate several times, usually at intervals of a week or two, or in severe cases, at intervals of a few days.

Sometimes the pericardial sac is partially filled with air intentionally after fluid has been removed (Figure 136, page 712) with the idea of allowing resolution of the acute pericardial inflammation to occur with less likelihood of the formation of crippling adhesions during convalescence, but this procedure has not yet proved to be particularly successful.

Acute pericardial tamponade due to hemorrhage from trauma needs rapid relief by surgery to repair the heart wound along with transfusion of whole blood. Intravenous infusions have been found beneficial preoperatively in acute pericardial tamponade (Cooper et al., 1944)

Differential diagnosis. Acute pericardial disease is often missed altogether because of absence or inadequacy of symptoms or signs, predominance of the underlying disease, or hasty or careless examination. There are four conditions which are most likely to be confused with acute pericardial disease (1) cardiac enlargement, (2) acute myocardial infarction, (3) the presence of harsh heart murmurs, and (4) acute abdominal disease.

The fast development of pericardial effusion, the frequent presence of a friction rub, and the absence of particular reason for sudden cardiac dilatation generally distinguish without difficulty pericardial disease from cardiac enlargement, but in some cases the distinction is impossible, and in still other cases there is a confusing combination of pericardial effusion and cardiac enlargement in the same individual. The electrocardiogram is often helpful in the differentiation.

The frequent possibility of the confusion of acute infectious pericarditis, especially the "idiopathic" kind in young male adults, with cardiac infarction has become increasingly evident of late years, and the importance of this error especially as regards prognosis, can hardly be overemphasized. The prolonged and often severe precordial pain, fever leukocytosis, pericardial friction rub and common appearance of abnormalities in the electrocardiogram in acute infectious pericarditis may easily simulate the findings in acute cardiac infarction. There are certain clues, however in the differentiation of the two conditions, chief of which is the fact that infectious pericarditis itself is almost invariably painful, with much aggravation of the pain on inspiration, due in part to the common coexistence of a pleuritis (in fact, the process is as a rule really a pleuropericarditis) while the pericarditis associated with myocardial infarction is per se (being visceral) painless, the severe pain of the muscle involvement being uninfluenced by respiration and subsiding as a rule by the time the friction rub appears. Other clues are the difference in the electrocardiograms (see above) the frequent development of some degree of pericardial effusion, and the younger age of the majority of the cases of acute pericarditis.

Very rarely does the character of the pericardial friction rub resemble that

of a heart murmur but it may be necessary in a few cases to wait to see if the uncertain sound persists, disappears, or becomes more definitely one thing or the other

Pain of acute pericarditis referred to the abdomen, or hepatic engorgement due to an acute or subacute pericardial effusion, may occasion a mistaken diagnosis of acute abdominal disease, especially in children, laparotomy has been done in some such cases for supposed acute appendicitis or other lesion

Rare causes of mistaken diagnoses include localized or encapsulated pericardial effusions which may be taken for aortic aneurysm, mediastinal tumor, or dilated left atrium a pleural friction rub may be wrongly called pericardial. Careful study generally simplifies the differentiation.

B CHRONIC PERICARDITIS, INCLUDING CHRONIC CONSTRICTIVE PERICARDITIS (PICK'S DISEASE)

One of the most difficult of all clinical cardiovascular diagnoses is that of chronic pericarditis. Fortunately it is for the most part of little or no importance. Frequently it produces neither symptoms nor signs.

Etiology *Cause* The causes of chronic pericarditis are acute pericardial inflammation of rheumatic, tuberculous, septic, or other often unknown, infectious origin and cardiac infarction (from coronary thrombosis) neoplasms, and hemopericardium from trauma. The commonest known cause is the rheumatic infection, and next comes pulmonary and pleural disease. Often the cause is obscure the antecedent acute inflammation having escaped notice. On occasion tuberculous, pneumonia, polyserositis (Concato s disease, Concato 1881) and the influenzal infection, and rarely some septic infection, are known to be responsible for chronic pericarditis. Trauma resulting in hemopericardium may leave chronic adhesive pericarditis.

At the Mayo Clinic (Smith and Willius, 1932) 144 cases of chronic adherent pericarditis were found among 373 cases of pericardial disease (38 4 per cent) rheumatic fever was apparently the etiologic factor in 21.5 per cent, pulmonary and pleural disease in 17 4 per cent, cardiac infarction in 6.2 per cent, neoplasms in 2.8 per cent, and tuberculosis in 2.1 per cent, while in the remainder (50 0 per cent) the cause was not evident.

Age Although the greatest incidence of this pathologic condition is in middle age, chronic pericarditis may exist at any age between 10 and 60 years. The average age is about 35 years.

Sex. Males are more often affected than females, in the ratio of 2 or 3 to 1

Pathology Following acute pericarditis of slight degree the healing process may leave but little thickening or scarring on more or less extensive areas of the pericardial surface without adhesions between the surfaces (parietal and visceral) but when the active process is extensive or of long duration adhesions of considerable extent result. Thus, chronic pericarditis may be divided pathologically into five groups. *First* there is simply slight scarring consisting of thickening and fibrosis of the pericardial surface usually in small areas.

without adhesions and without any effect on heart size or function. The well-known "milk spots" or "soldier's patches" probably belong in this category although their etiology is obscure. As a matter of fact pericardial milk spots are common, about one third of all persons over a year old showing them at autopsy (Nelson, 1940) they are scarce in children but very common in old age two thirds of individuals with chronic valvular disease have them and half of those with coronary heart disease. *Second* there are slight, loose, localized pericardial adhesions of fibrous tissue, also without effect on the size or function of the heart. *Third*, there are the cases of complete but not dense adhesion between the visceral and parietal pericardial surfaces without firm fixation to chest wall, diaphragm, or mediastinum. In such cases the adhesions are often loose and the pericardium is but little thickened so that there is no handicap to the heart in its function and no cardiac enlargement. *Fourth*, there is *concretio cordis* (a hardening of the heart) when the pericardial adhesions are solid, thickened, and even calcified. For such instances in which the heart function is impeded and the inflow of blood from the great veins obstructed (Figure 138 page 724) the best designation is *chronic constrictive pericarditis*; this condition may follow a polyserositis of unknown cause, it may result from pneumonia, but in most cases it is probably of tuberculous origin Rarely the visceral and parietal pericardial layers may be densely thickened and unyielding but without complete adhesion. Often in these cases the heart is adherent to the diaphragm, a further handicap *Fifth* the adhesive pericarditis may be complicated by an extension of the process to the mediastinum and chest wall so that the heart itself is anchored in every direction by firm fibrous tissue (*chronic mediastinopericarditis*) with much extra work and some enlargement of the heart resulting.

The factors responsible for the fourth and fifth groups, that is, constricting and anchoring adhesions, are often present in the same case. In fact it is usually difficult or impossible to separate these two groups, the fourth and the fifth in general they might best be considered as one, although there are exceptions. The only important cases of chronic adhesive pericarditis demanding especial attention belong here.

Occasionally lime and rarely even bone are deposited in chronic pericardial adhesions when they are especially thick and massive.

It is of much interest that long before Pick (1896) and even before Kussmaul (1873) the effect of chronic constrictive pericarditis on the heart and circulation was well understood by Chevers (1842) and Wilks (1870) at Guy's Hospital in London.

Chevers, N "Observations on the Diseases of the Orifice and Valves of the Aorta. *Guy's Hosp. Rep* 1842, VII, 387

"The principal cause of dangerous symptoms in cases of the above description [with much thickened constricted pericardium and obliterated sac] appears to arise from the occurrence of gradual contraction in the layer of adhesive matter which has been deposited around the heart, compressing its muscular tissue, and

embarrassing its systolic and diastolic movements, but more particularly the latter. Under these circumstances, the circulation seems, after a time, in great measure to adapt itself to the encumbered condition of the heart. The ventricles, having become diminished in capacity make up for this loss by the rapidity of their contractions (hence the small and rapid pulse, noticed in the above case) while the main arteries, if not already diseased, adapt themselves to the dimensions of the



FIG. 138. Photograph of heart encased in thickened, leathery constrictive pericardium. Case of chronic constrictive pericarditis (so-called Pick's disease)

cavities from which they arise. And thus the blood passes onward, for a time, with tolerable freedom but the patients become incapable of continued muscular exertion, and are always liable to suffer from dropsy and other serous effusions, upon the occurrence of very slight pulmonary obstructions. In the case which I have quoted, the serous effusions which gave rise to the most prominent symptoms of disease evidently arose from the cavities of the heart being no longer capable of transmitting the blood with ordinary freedom. The heart had, doubtless, for a long time continued to become more and more compressed, weakened, and embarrassed, by the gradual contraction of the adventitious structure which surrounded it. distension of the great veins and abdominal viscera had necessarily followed, and the resulting anasarca and ascites must have added still more to the obstruction with which the already almost powerless heart had to contend.

Chronic mediastinopericarditis may be at times very complicated, causing obstruction of the great veins, the superior vena cava, inferior vena cava, and even the hepatic veins by kinking and compression, but particularly constriction and anchoring of the heart chambers themselves. It is the hepatic vein obstruction *secondary* to the constriction of the heart itself, with or without an additional factor of local blocking, that leads to hepatic congestion, enlargement, and eventual cirrhosis called *mediastinopericarditic pseudocirrhosis of the liver* or *Pick's disease* (Pick, 1896) It should be added that this last-named condition may or may not be associated with polyserositis (Concato's disease) and perihepatitis ("icing" or "frosting" of the peritoneum over the liver due to chronic peritonitis) these two different conditions, that is, mediastinopericarditis and polyserositis, have often been confused in the past, since it is true that the former condition may result from the latter Chronic mediastinopericarditis may involve the superior vena cava even more than the inferior vena cava in cases of the superior mediastinal (pressure) syndrome, but usually the inferior vena cava and hepatic veins are equally or more affected (inferior mediastinal syndrome) as a matter of fact the condition is usually a total mediastinal syndrome The right heart chambers are more often seriously constricted than are the left heart chambers, though there are many exceptions. The liver rarely shows more than vascular congestion with very little cirrhotic change a few cases progress to or are complicated by a moderate degree of hepatic cirrhosis. However there are seldom, if ever the marked changes found in the usual cases of portal cirrhosis.

Pick, F "Über chronische unter dem Bilde der Lebercirrhose verlaufende Perikarditis (*perikarditische Pseudoleberecirrhose*) *nebst Bemerkungen über die* Zuckergussleber (Curschmann) *Ztschr f klin. Med.*, 1896, XXIX, 385

Pick described three cases (including the postmortem examination) of what he called pseudocirrhosis of the liver resulting from chronic adhesive pericarditis involving the mediastinum. The sex and age of these three cases were as follows male of forty-seven years, male of twenty-six years, and male of twenty-four years. In the third case tuberculosis was the etiologic factor behind the pericarditis, in the second case tuberculosis was the probable factor and in the first case the cause was unknown.

His first sentences and his conclusions I have translated as follows.

"To differentiate clearly between primary and secondary disease of the liver is very difficult in occasional cases where liver enlargement with more or less ascites eventually leads to cirrhosis. This is especially the case if there are no well-marked physical signs of a heart lesion or of circulatory stasis in the upper part of the body

Conclusions

1 There is a symptom complex of *pericarditic pseudocirrhosis of the liver* which is deceptively similar to one of the mixed forms of hepatic cirrhosis with enlarged liver and considerable ascites but no jaundice. This pseudocirrhosis of the liver is caused by disturbances of the circulation of the liver due to latent pericarditis. These circulatory disturbances lead to an increase in connective tissue (fibrosis or cirrhosis) which in turn causes stasis in the portal circulation with marked ascites.

2 This symptom complex is found preponderantly in young individuals but it may be observed also in later periods of life.

3 The following points are important in the differential diagnosis (a) absence of an etiologic factor for cirrhosis of the liver (b) history of a previous pericarditis, and (c) earlier occurrence of edema of the legs. Certainty can come only through subsequent examination of the heart.

Symptoms. There may or may not be symptoms from chronic pericarditis Usually there are none since cases of the first three unimportant pathologic groups discussed above are much more frequent than of the last two important groups. Clinically chronic pericarditis may be divided into four groups (1) that with unimportant adhesions or none at all, which comprises the first three pathologic groups (2) that of an important degree of constrictive pericarditis without external adhesions, (3) that of significant external adhesions, to chest wall and mediastinum with little or no constriction of heart or great veins, and (4) that of groups 2 and 3 combined to a greater or lesser degree. It is unlikely that from uncomplicated external pericardial adhesions per se the heart is ever exhausted by the strain of tugging in the chest wall or of pulling up the diaphragm with each contraction when heart muscle failure develops in the presence of adhesive pericarditis there is always to be found other more adequate cause for the failure, especially aortic or mitral valvular disease the pericardial adhesions may of course, add a minor burden in addition but it seems to be relatively unimportant. When, on the other hand, the heart is so compressed that there is insufficient blood flow activity is usually much limited, abdominal discomfort and distention result from hepatic congestion and ascites, and there may be also dyspnea and weakness.

Signs. As is the case with symptoms, so there may be no signs whatsoever of chronic pericarditis, unless the pericardium is extensively adherent or constrictive. The usual absence of important adhesions clearly explains why the diagnosis is so often missed during life.

A frequent finding in chronic adhesive pericarditis is cardiac enlargement but this is inconstant and not diagnostic, and almost always there are other lesions, especially valvular defects, that are much more important causes of

the enlargement. Cardiac enlargement is not present unless extra work has been required of the heart because of adhesions to chest wall, diaphragm, or mediastinum. The enlargement is due to a combination of hypertrophy and dilatation. Years ago it was reported (Cabot, 1926) that the largest hearts of a certain series of cases were the result of chronic pericarditis but a careful survey of these cases showed that aortic valve defects (and not the pericarditis) were the real cause of the enlargement (White, Sprague, and Jones, 1926) Increased heart size was found in 29 (55 per cent) of a series of 53 cases of chronic constrictive pericarditis (Paul, Castleman, and White, 1948)

There are two signs which are more or less distinctive of chronic pericarditis of the more serious types. The first is the fixation of the heart by adhesions in some cases physical examination and roentgen ray study show little or no change in the position of the heart with change in body position (upright, recumbent, right lateral position, left lateral position) or respiration (full inspiration and full expiration) Electrocardiography is of least value in studying the extent to which the heart is anchored (see Chapter 9) Fixation of the heart to the sternum causes the heart to rise rather than to descend with *inspiration, with retraction of the lower end of the sternum at the same time.* Also the fixation of the heart and pleural edges may prevent any change of pulmonary resonance over the heart between full inspiration and full expiration. The pleural edges are at times somewhat retracted from over the heart, increasing the area of absolute percussion dullness. Such definite fixation is, however found in relatively few cases Other confirmatory signs of extensive pericardial adhesions are inconclusive in themselves, they include especially a systolic retraction of the chest wall, particularly in the left axillary region and left back, involving the ribs as well as the intercostal spaces (Broadbent's sign) and probably due to fixation of heart to diaphragm. Although this sign is sometimes also seen when the heart, especially the right ventricle, is very large without any adhesions, it is seen best in cases of adherent pericardium.

Broadbent, John F H. *Adherent Pericardium*. London, 1895

In Chapter II the section on Physical Signs of Adherent Pericardium begins as follows

"The physical signs differ according as the adhesions exist only between the two layers of pericardium or between the pericardium and chest wall, or adjoining pleura, as well. In the latter case they are more numerous and distinctive, and will therefore be first discussed.

P 26. *Retraction f the Posterior Lateral Portions of the Thoracic Walls* In cases of adherent pericardium, marked systolic retraction of some of the lower ribs on the lateral or posterior aspect of the thorax may sometimes be seen. This phenomenon is best seen when the patient is sitting up in good light, and the movements of the chest are carefully observed from a short distance off, first from the front, and then from the lateral aspect. When a pulsatile movement is seen over the lowest part of the left side of the chest posteriorly it may at first sight appear to be expansile. On a more careful scrutiny it will be found that there is a tug on the false ribs during the cardiac systole and a sharp rebound during diastole

which can be felt as well as seen when the hand is laid flat upon the chest wall at the spot. It is more marked when a deep inspiration is made. It may be seen occasionally not only on the left side but also on the right, especially if the patient leans over to the left.

Here, it is not possible that the heart can be directly fixed to the chest wall at the points of retraction by pericardial adhesions, as the lung tissue intervenes, but the explanation seems to be the following. The heart is, by means of the pericardium, adherent not only to the central tendon of the diaphragm but probably also to a large area of the fleshy or muscular portion of the diaphragm, and, it may be, to the anterior thoracic wall as well; as it contracts it drags upwards and inwards the less resistant fleshy part of the diaphragm towards the central tendon or anterior chest wall; hence the points of attachment of the digitations of the diaphragm to the lower ribs and costal cartilages are dragged inwards and downwards. It will always be found in such cases that the retracted positions of the chest wall correspond to the floating ribs or costal cartilages of the lower ribs *at the points of attachment of the diaphragm. (Systolic recession of the left subcostal angle and epigastrium does not necessarily imply the presence of pericardial* adhesions.)

"The above is a most important diagnostic sign of adherent pericardium when present, and is quite distinct from recession of the lower ribs in inspiration.

The other important and distinctive finding on physical examination occurs in cases of constrictive pericarditis due to the small amount of blood that can enter and therefore leave the heart because of the cardiac compression. This finding consists of increase of systemic venous pressure even up to 20 or 30 cm of water (normal 6 to 8 cm) with engorged neck veins and hepatic engorgement (and in late cases slight cirrhosis) and ascites alone or out of all proportion to the degree of dependent edema in the legs (Figure 139), accompanied by low arterial pulse pressure, often so small that the radial pulse almost disappears on deep inspiration (marked paradoxical pulse). This evidence is the clearest indication that we possess of an important degree of chronic pericarditis, when linked with the finding of a relatively normal heart, without valvular disease, with little or no enlargement, and with limited diastolic excursion as noted by roentgen ray study. The pulsation of the right heart border is more often embarrassed than is that of the left.

There is one sign, a rare one, which is pathognomonic of chronic pericarditis and that is the evidence by roentgen ray of calcification of the pericardium (Figure 140, page 730). Pericardial calcification may or may not be attended by constriction of the heart. It was present in 29 (55 per cent) of 53 cases of chronic constrictive pericarditis (Paul, Castleman, and White, 1948). Roentgen ray examination also infrequently shows actual irregularities of the contour of the cardiac shadow due to the pull of adhesions.

Very helpful confirmatory evidence of chronic constrictive pericarditis is electrocardiographic. There is invariably either low voltage of *QRS* waves (60 per cent) *or inversion of T waves (all cases) or* both (Figure 141, page 731). These abnormalities are also frequently found in cases of acute constrictive pericarditis.

There are ordinarily no characteristic changes in heart shape and no murmurs or arrhythmias except as they develop as complications. A systolic murmur at the apex is frequent with enlargement and is due to functional mitral regurgitation. Very rarely there may be also a mitral diastolic murmur at the apex without mitral or aortic valve disease, due simply to left ventricular

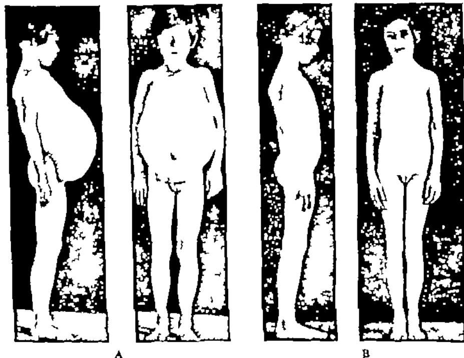


FIG. 139 Photographs of young girl with chronic constrictive pericarditis (so-called Pick's disease) (*A*) during her disability (*B*) one and one-half years after her surgical cure.

dilatation resulting from the pericardial adhesions. A frequent finding in chronic constrictive pericarditis, both before and after pericardial resection, is a loud third heart sound, especially well heard at the left lower border of the sternum, which may be explained by right ventricular dilatation when the left heart chambers are more constricted than the right or the right ventricular myocardium weak and atrophic. Atrial fibrillation is common in the cases of chronic constrictive pericarditis (Pick's disease) and atrial flutter also may occur; these arrhythmias were present in 20 (38 per cent) of 53 cases of chronic constrictive pericarditis (Paul, Castleman, and White, 1948). The blood pressure and pulse pressure are low if the blood flow is much reduced by the hampering of the heart action.

In a case with chronic constrictive pericarditis of long standing and attended by malnutrition the blood serum protein is often reduced to below 5 gm per cent and the albumin-globulin ratio may be reversed, favoring an increase in





IG. 140. Roentgenograms of thorax of O.P age 45 with chronic constrictive pericarditis, showing calcification of the pericardium. (A) Anteroposterior view (B) right anterior oblique view

edema, such a finding is due probably in part to the malnutrition, in part to the loss of protein in the ascitic fluid, and in part to the reduced liver function. There is usually but little anemia.

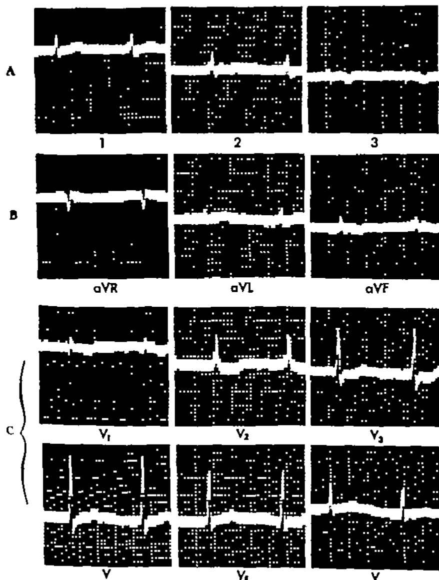


FIG. 141 Electrocardiogram in chronic constrictive pericarditis, male, age 50. (*A*) Bipolar limb leads 1 2, and 3 (*B*) unipolar limb leads, VR, VL, and VF (*C*) six precordial leads, V to V inclusive. Note especially the low voltage of the *QRS* waves in all the limb leads and the very low or inverted *T* waves throughout. Despite the regular ventricular rhythm the *P* waves are not made out. Time = 0.04 and 0.20 second; amplitude 1 mm = 0.10 mv

One of the most interesting varieties of chronic constrictive pericarditis which leads to pulmonary hypertension and right ventricular enlargement, acting much like mitral stenosis, consists of preponderant involvement (constriction) of the left heart chambers, especially the left atrioventricular groove; cardiac catheterization helps to confirm the pulmonary hypertension (White, et al. 1948) a special surgical approach can correct this, as noted on page 735

Course and prognosis. In the less important types of chronic pericarditis there is usually no interference with the normal duration and activity of life, except as complications like valvular disease may affect the prognosis. In many cases the pericardial adhesions are discovered only at postmortem examination in patients who have never had any cardiac symptoms or signs and have died a noncardiac death. Even the original acute pericardial illness may be unsuspected or untraced. The more marked cases however especially those with constrictive pericarditis generally develop symptoms and signs of heart failure or of systemic venous congestion with hepatic enlargement and ascites in youth. With crippled lives they may survive for many years, but finally usually in middle age, they gradually fail and die from the effects of the pericarditis itself or from complications, unless they are relieved by pericardial resection which affords much help or even cure in about half the cases.

Complications. The most frequent complications of chronic pericarditis have already been mentioned systemic venous congestion with hepatic enlargement and ascites, and chronic valvular disease (in about half the cases) Hypertension, coronary disease, and bacterial endocarditis are infrequently associated with pericardial adhesions. Atrial fibrillation is found occasionally Pleural adhesions are commonly associated with adhesive pericarditis, the result of a mutual polyserositis in the past, there may be chronic constrictive pleuritis as well as chronic constrictive pericarditis (Burwell and Ayer 1941)

Treatment. There is no need of any particular treatment in most cases of adherent pericardium even if the condition is recognized, but there are two important surgical procedures, both called cardiolysis (καρδία, heart, and λύειν to free) which are indicated in certain cases. These are (1) rib removal (thoracolysis) when there are extensive adhesions to the chest wall, and (2) pericardial resection, or cutting away of pericardium, when there is compression of heart or great veins.

Rib removal. The simpler chest wall operation, called Brauer's operation (Brauer 1902) consists of the removal of several ribs and costal cartilages (usually three) on the left side over the precordium for a distance of about 10 to 15 cm from the sternum. It quite probably can relieve the heart which is adherent to the chest wall of some, at least, of its extra work. This operation has also been suggested and done in rare cases of marked cardiac enlargement without pericardial adhesions to relieve the heart of the task of displacing the anterior chest wall forward at each systole· although it has not been generally adopted, several patients have apparently experienced some subjective relief, that is, relief from the discomfort of the forceful heart action. The operation

has been performed but little for adhesive pericarditis and now has for that purpose been largely abandoned since the Delorme operation of pericardial resection has widely and justifiably supplanted it· indeed in former days before the diagnosis of crippling chronic pericarditis was made with any degree of accuracy the Brauer operation was done in some cases that proved to have marked cardiac enlargement with no pericarditis at all.

As a matter of fact, freeing the heart from extensive adhesions to chest wall or diaphragm would be much better carried out in these modern days of enlightened thoracic surgery by splitting the sternum medially lengthwise without permanent deformity of the chest such as follows Brauer's operation.

Brauer L. "Ueber chronische adhäsive Mediastino-Perikarditis und deren Behandlung. *Münch. med. Wchnschr* 1902, XLIX, 1072.

"Die Erfolge der Kardiolysis. *Ibid.*, p 173..

Two discussions of cardiolysis for adhesive pericarditis took place at the Naturhistorischmedizinischer Verein in Heidelberg, May 13th and July 18th, 1902. The official report of the first of these two sessions is as follows (the translation is by myself)

"The speaker [Brauer] demonstrated two cases of chronic adhesive mediastino-pericarditis and described in relation to these cases the etiology and diagnosis along with the expected further course and the pathologic structural changes doubtless present.

"Both patients showed in the most striking manner a systolic retraction of the lower anterior chest wall alternating with a vigorous diastolic rebound. A collapse of the cervical veins was also evident during cardiac diastole. The diastolic rebound of the chest wall was accompanied by a ringing tone which masked the usual second heart sound. Kussmaul s signs of the pulsus paradoxus and of inspiratory dilatation of the neck veins were absent.

In both cases there were signs of myocardial disease with enlargement of the liver and evidence of massive circulatory stasis.

"Since a significant increase of the work of the heart was caused by the systolic pulling in of the chest wall which rebounded immediately in diastole with so much force, the speaker decided to free the heart by making a break in the bony ring of the thorax by the resection of ribs. Through this procedure the heart would contract with the pulling in no longer of the elastic ribs but simply of a covering of the soft parts of the chest wall.

Professor Petersen had happily brought about this result in one of these two patients by resecting the ribs covering the heart.

"The consequence of this operation described above and carried out on the first day of April, 1902, was very satisfactory The patient is both subjectively and objectively much improved. Similar treatment in the case of the second patient will therefore be considered.

At the second session in July the following report was made

"Following his intention t the assembly of the 13th of May 1902 (this journal, No. 25) the speaker [Brauer] demonstrated the second of the two patients shown previously

"Dr Simon had performed the operation on this patient which the speaker

had recommended. This time a considerable part of the sternum was resected with the ribs.

"The expected result followed. The patient, whose heart no longer was obliged to pull in the entire anterior bony chest wall with each contraction, but only a yielding surface, improved appreciably found that he could move more freely with less dyspnea, and was almost completely rid of signs of cardiac insufficiency which had been threatening him."

Brauer L. "Die Kardiolysis und ihre Indikationen. *Arch. f klin. Chi* 1903, LXXI 258.

(Translation by myself)

About a year ago I described under the name of cardiolysis a method for the surgical treatment of adhesive mediastinopericarditis.

"Today I hope to be able to demonstrate to you the expediency of the procedure through the progress of both the cases which were reported at that time. In the meantime, since the early reports, a third case has been operated upon and new observations have been made on the differential diagnosis and the determination of those cases which qualify for the operation.

Moreover since one of the patients died a year after the operation from the accidental complication of an influenzal pneumonia, the opportunity has been afforded to orientate the characteristics of the disease picture with the actual anatomical preparation and to discuss the different possible operative procedures.

"The most important indication for cardiolysis is afforded by those forms of adhesive pericarditis which cause a systolic retraction of a broad area of the thorax. So long as vigorous thoracic movements of this sort are demonstrable, a good result may be expected.

Finally with what aim should one operate? Is it necessary actually to free the adhesions or sufficient merely to restore freedom of action for the heart by simply resecting ribs or sternum? The former procedure has been recommended by Delorme and by Beck [New York] but apparently it has not yet been accomplished. It appears to be a very extensive procedure and it may be questionable whether or not one should subject the patient to it at all. All this must first be ascertained through further coöperative work of surgeons and internists."

The apparent operative success reported by Brauer may have actually been due, in part at least, to the breaking of a constricting cuirass around the heart in the course of freeing that organ from the chest wall, even though there was no specific decortication.

Pericardial resection. The other operation, mentioned above by Brauer more truly a freeing of the heart or cardiolysis consists of precordial rib removal with resection of the left side of the sternum whereby the pericardium and heart are exposed, followed by the actual cutting away of as much of the thick constricting pericardium from the heart surface as is possible at the time, with the resection also of any constricting bands about the great vessels especially such as may involve the inferior vena cava under the sternum (Delorme, 1898) An expert and experienced surgeon must be selected to undertake this difficult operation and anesthesia must be carefully admin-

listered. The operation is better postponed, if possible, until after the acute stage of any tuberculous pericarditis. The younger and fitter the patient, the less is the risk and the more likely is marked improvement to follow

Delorme, Professor "Sur un traitement chirurgical de la symphyse cardiopéricardique. *Bull. et mém. d. l. Soc. d. chir. d. Paris*, 1898, XXIV 918.

(Translation by myself)

If the surgeon feels legitimate regrets in publishing a method of treatment which he has conceived but been unable as yet to apply on the other hand he risks the loss of the advantage of the original idea and the compromise of its application if he waits too long. It is to avoid this last difficulty that I have resolved to speak to you of a surgical treatment of cardio-pericardial adhesions concerning which I deposited a confidential note in 1895 at the Academy of Medicine and the application of which I have been unable to effect, despite repeated appeals to my colleagues of the medical services of the Val-de-Grace Hospital. This treatment consists of the resection or destruction of the cardio-pericardial dhesions.

Already a considerable number of striking cases of relief and cure following pericardial resection have been reported, as in the case of the child shown in Figure 139 page 729 (Rehn, 1920· Sauerbruch, 1925 Churchill and White, 1929 1930, White, 1935 1942 with Harrison, and 1948 with Alexander and Sweet, and with Paul and Castleman Blalock and Burwell, 1935 1941 Beck, 1931 and 1943) Of our own series of 53 cases 42 were subjected to this operation, 25 (60 per cent) were cured or much improved, 16 patients died, 6 as the result of the operation itself, 5 from complicating diseases, 4 from the pericarditis itself, and one of unknown cause· 7 of the 11 cases not operated upon were too ill for surgery and 2 others did not need it (Paul, Castleman, and White, 1948) One of our cured cases is illustrated in Figure 139 page 729) In September 1950 Dr C. S. Beck of Cleveland kindly wrote to me of the results of pericardial resection in his series of 61 patients 38 patients (62 per cent of the entire group) were classified as clinically cured. Ten others were somewhat improved and two cases showed no improvement. One patient died on the table and ten others during the postoperative period or later

The further development of the surgical treatment of serious chronic pericarditis is a promising field for the future. An important step forward has consisted of a new surgical technic consisting of a lateral thoracic approach allowing exposure of both back and front of the heart or better still, of the splitting of the sternum which allows the chest to be widely opened with less later mutilation of the chest. By either of these approaches, important degrees of constriction of the left heart chambers can be cleared by posterior pericardial resection done prior to that over the anterior heart chambers, such an approach is indicated when there is evidence of pulmonary hypertension as presented on page 732.

Medical treatment of chronic pericarditis is obviously less hopeful, although it may aid considerably in combating the complications, especially the venous congestion due to chronic constrictive pericarditis. The treatment of congestive heart failure in cases of serious heart disease, especially with valvular deformities, complicated by chronic pericarditis with or without important external adhesions, is discussed in Chapter 30. The medical treatment of venous congestion in chronic constrictive pericarditis may be briefly summarized as follows limited activity with much rest, diet low in salt, limited to 1 gm or less of sodium daily diuretic drugs by mouth and intravenously exactly as for congestive failure (see Chapter 30) and paracentesis of abdomen and thorax as needed. When the blood serum protein is low a high protein diet is somewhat helpful Digitalis in chronic constrictive pericarditis is ineffective in controlling the congestion, though it is very useful in controlling the heart rate when there exists the occasional complication of atrial fibrillation at one time, as in 1937 when the second edition of this book was published, it was thought by some, including myself that a slow pulse in this disease might actually be harmful and that a relatively fast pulse should help to compensate, so far as the blood flow is concerned, for the small output of blood per beat, but careful observation during the past decade has shown this not to be the case, most of the patients being considerably better with slower pulse rates, under digitalis therapy than with rates approaching or exceeding 100 per minute.

Omentopexy (Talma operation) is contraindicated in chronic constrictive pericarditis, since it in no way affects the fundamental condition.

To prevent the development of pericardial adhesions in the course of acute pericarditis, injections of air and oil into the pericardial sac have been suggested and made, but such procedures have not yet been proved useful.

Differential diagnosis. When chronic pericarditis with external adhesions produces any signs at all, it must be differentiated from cardiac enlargement per se, from any cause, with or without congestive failure. This can be done in a few cases where the heart is clearly fixed in position and where other etiologic factors like hypertension and valvular disease are absent. When other causes are combined with chronic adhesive pericarditis to produce cardiac enlargement and failure it is usually easy to diagnose the other causes and to miss the pericarditis. Broadbent's sign may be misleading, being found in some cases of marked cardiac enlargement, especially of the right ventricle, without adhesive pericarditis, the retraction of the heart from the chest wall during systole simulating the tug of pericardial adhesions. And, as noted above, chronic pericarditis, even with calcification, may be present without any cardiac enlargement or constriction at all.

A previous history of acute pericarditis is naturally of great value in the diagnosis of pericardial adhesions.

Chronic constrictive pericarditis causing enlargement of the liver with ascites (Pick's disease) must be differentiated from true cirrhosis of the liver. This can usually be done easily there are two clearly distinguishing points,

both to be found in the case of chronic constrictive pericarditis (1) engorgement of the neck veins and (2) abnormality of the electrocardiogram.

It is also to be remembered that marked chronic mitral stenosis, with or without tricuspid valve disease, may itself be a cause of chronic hepatic congestion, but in such a case the mitral diastolic murmur and other evidences of the mitral stenosis and tricuspid insufficiency are present.

The usually insidious onset, the liver engorgement with preponderant ascites (as compared with dependent edema) the increased systemic venous pressure (as shown by the neck veins) with relatively normal heart, and the abnormality of the electrocardiogram are the clues which in combination make the diagnosis of chronic constrictive pericarditis certain.

Finally chronic constrictive pericarditis is not polyserositis, although it may follow it.

C. CONGENITAL PERICARDIAL DEFECTS

There are three types of pericardial abnormality of congenital origin, all rare. These are absence or defect of the parietal pericardium, diverticulum or hernia, and lack of attachment of the pericardium. For a discussion of these and bibliography the reader is referred to Chapter 13

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CHAPTER 28

VASCULAR DISEASE
DISEASES OF THE AORTA AND PULMONARY ARTERY
PULMONARY EMBOLISM
ANEURYSMS
DISEASES OF ARTERIES AND VEINS

Vascular disease like heart disease itself has seen a good many advances during the past seven years since the last edition of this book, especially in the fields of diagnosis and surgical therapy but only the most important of these advances can find a place in this fourth edition.

Blood vessel abnormalities make up an important part of the study of cardiovascular disease, not only from the standpoint of the circulation as a whole but also from that of the heart itself Many vascular disturbances are of functional nature, due to abnormal dilatation or constriction of arteries and capillaries, and these will be discussed in Chapter 31 (Part IV Disorders of Cardiovascular Function) Structural vascular changes as they affect the heart and great vessels will be considered in the present chapter Diseases of the peripheral circulation per se, however will be discussed but briefly in the present edition in order to save space in this expanding book which deals primarily with diseases of the heart and great vessels. Many of the newer significant references to publications on peripheral vascular disease have, however been added to the Bibliography and the reader is also referred to the newer textbooks on the subject.

DISEASES OF THE AORTA

Organic disease of the aorta is exceedingly common but fortunately it is of little or no importance in the majority of cases. Some change of the aortic wall is almost universal after the age of forty years.

ACQUIRED AORTIC DISEASE

Etiology *Cause* There are four chief types of acquired aortic disease (1) atherosclerosis, the most common type, (2) dilatation due to hypertension or aortic regurgitation, (3) infectious changes, and (4) rarely traumatic lesions Besides these types there are occasional instances of aortic disease of unknown nature.

The first and commonest lesion, called atherosclerosis, is found in considerable degree in old age but begins often in youth. The cause of the abnormal deposition of cholesterol fat droplets and crystals in the intima of the aorta which constitutes atheroma is still unknown, whether a fault in fat metabolism or of local tissue function or of other nature much study of these factors is needed to solve this very vital problem. Heredity is the only recognizable factor that is fairly consistent, it seems likely that several factors (especially heredity local strain, and disturbed fat metabolism) may combine to cause atheroma.

Dilatation of the aorta of moderate degree is a common result of chronic hypertension and of well-marked aortic regurgitation, and in rare cases is due in old age to a loss of elasticity with resultant senile ectasia (*ἔκτασις*, a stretching out)

Infectious aortitis is frequently seen in youth and middle age, most commonly and typically as a late manifestation of syphilis, but it is also occasionally found as an acute lesion (called mycotic) in other infections such as rheumatic fever typhoid fever and tuberculosis. Saccular aneurysms are almost invariably the result of syphilitic aortitis.

Traumatic lesions, the result of direct or indirect trauma (perforation, blows, strain) occur as a rule in the case of an aorta already diseased, most commonly by syphilis, atheroma, or medial necrosis of unknown cause. If the trauma is indirect it occurs usually at the time of the greatest distention of the aorta.

Medial necrosis and hypertension combined, with or without the additional element of trauma, give rise in rare cases to a very important lesion consisting of a splitting of the aortic wall, called a dissecting aneurysm.

Age Naturally the great preponderance of aortic disease is found in older persons, after the age of 45 years, because hypertension and syphilitic aortitis are then more advanced, and because atheroma is especially a senile change. Atherosclerosis has, however been noted frequently in otherwise healthy individuals between the ages of 30 and 50 years and sometimes even in children and youths. On the other hand, the aorta, especially in the ascending portion, is often astonishingly smooth and elastic in individuals over the age of 75 years, in fact this appears to be the rule in persons who live to be very old It may be evidence of the inheritance of good arterial tissue. Infectious aortitis is commonest in young and middle-aged individuals, syphilis being the chief factor between 40 and 50 years of age.

Sex The male sex is more often the victim of aortic disease than is the female in the proportion of about 2 to 1

Pathology *Atheroma* (ἀθήρη, crushed grain or porridge) begins as a deposition of cholesterol fat in the intima where it appears engulfed in lipoid

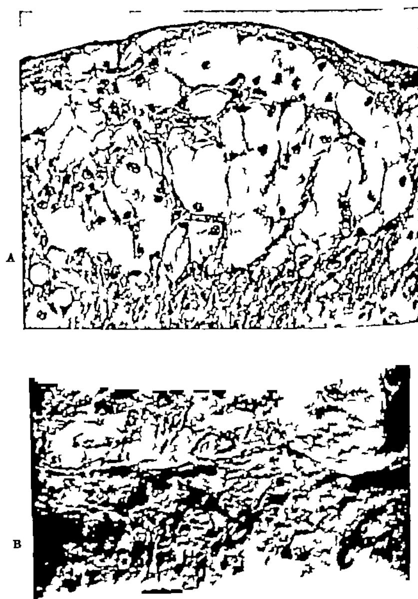


FIG. 142. Photographs showing aortic atherosclerosis. (*A*) Microphotograph showing atheromatous lesions of the aorta with cholesterol in the lipoid cells, grossly the lesion was pinhead-sized orange-yellow nodule. (Kindness of Dr Timothy Leary) (*B*) Atherosclerosis of thoracic aorta showing well-marked atheroma, calcification and resulting ulceration. (Jores *Arterien*. Kindness of Julius Springer Berlin.)

cells (Figure 142A) There are thus produced small fleck like areas which raise slightly the inner surface of the aorta, encroaching a little on the lumen. This encroachment in the case of the aorta is of little or no moment but in very small arteries it becomes important. Gradually these areas tend to increase in size and number discoloring the aortic intima yellow At first the process is reversible, the fat being taken up and away but finally there is a reaction of fibrosis in these areas in middle age or even in younger persons while in older individuals lime salts are deposited in them In either case stiffening results, to which the term sclerosis (σκλήρωσις, hardness) has been applied. The development of the whole process from softening to hardening has been called atherosclerosis. The aorta may eventually become more or less rigid and quite inelastic (Figure 142B) The atherosclerosis may then be a handicap, though not a serious one, to the circulation which is normally maintained in part by the elastic pressure of the aorta when it is filled with blood by ventricular systole. The calcified areas or plaques may break or cause ulceration of the endarterium, leading to intra-aortic thrombus formation. The descending aorta in thorax and abdomen is more often involved by the atherosclerotic process than is the ascending aorta—for unknown reason, but perhaps because it is less adequately supplied with vasa vasorum. Sometimes the descending aorta when it loses its elasticity becomes much elongated, tortuous, and even kinked (Roesler and White, 1931) and has been known indeed to cause mild attacks of subacute intestinal obstruction (Palmer 1942) associated with the arteriosclerosis of the descending aorta, especially the abdominal portion, nonsyphilitic saccular aneurysms now and again occur It has already been noted that in very old persons the aorta, especially the ascending portion, may be extraordinarily normal, resembling that of a young adult.

Infectious aortitis is mainly of two types, that in which the media or musculature is chiefly involved and that in which endarteritis is the primary lesion. Rarely invasion of the aortic wall occurs directly by extension of infection through the adventitia from contiguous lesions, as in the case of tuberculous lymphatic glands pressing against the aorta. Slight infectious lesions may heal without causing any structural defect but there are six abnormalities of the aortic wall that more or less frequently follow aortitis, especially of syphilitic origin. These six defects are (1) weakening of the aortic wall with loss of elasticity and dilatation (2) aneurysmal pouches· (3) rupture of wall, either partial or complete· (4) ulceration of the intima (5) thrombus formation on the inner surface of the aorta, usually over ulcerated areas, and (6) partial or complete obstruction of the mouths of aortic tributaries—coronary innominate carotid, subclavian, and intercostal arteries. The extensive infectious lesions in which a large percentage of the aortic wall is involved are almost invariably syphilitic in nature In such cases the ascending aorta is the chief site of the disease beginning a short distance (1 or 2 cm) above the aortic valve· the media is the coat affected, with destruction of muscle and elastic tissue, patchy whitening of the aortic surface with wrinkling, and secondary involvement of the intima (Figure 89 page 412 compare with

Figure 142B) The syphilitic lesion probably results mainly from occlusi of the vasa vasorum, but treponemata themselves are found in the aortic wal Small localized aortic lesions are sometimes the early stage of syphilitic aortit but often such lesions are due to other infection, either directly involving th intima or through embolic invasion of the media by way of the vasa vasoru Occasionally these localized aortic lesions are complications of bacteri endocarditis and infrequently they are seen in rheumatic infections, typho fever and tuberculosis. There may result ulcerations, small "mycotic ane rysms, and intra-aortic thrombi resembling valvular vegetations, which ma contain bacteria.

In the case of syphilitic aortitis the infectious process may also progre downward to invade the aortic valve and to produce a serious aortic regurgi tation (Figure 131 page 686)

Medial necrosis Small defects of the media of the aorta, due to necrosi of unknown origin, have become recognized as distinct from syphilitic o other well-known infectious lesions (Erdheim 1929) they are apparentl a factor in the production of dissecting aortic aneurysms.

Saccular and dissecting aneurysms of the aorta will be discussed later i the present chapter

Rupture of the aorta is a common sequel of weakening of the wall and aneurysmal dilatation, usually of syphilitic origin occasionally rupture results from dissection of the wall (dissecting aneurysm of the aorta) due to the combination of medial necrosis (of unknown cause) and hypertension, or even without the hypertension It may occur as a complication of congenital coarctation of the aorta, rarely rupture results from atheroma and in a few cases it is caused directly by trauma of a healthy aortic wall. The perforation may be very small, consisting of a minute devious tear through the dissected aortic wall or of a tiny point at the bottom of an aneurysm with slow or intermittent bleeding in very rare cases spontaneous healing may take place with or without recurrence later There may be a large linear tear often clean-cut as if with a knife, especially when there is no previous aortic disease; such a large tear results in a profuse, rapidly fatal hemorrhage Bleeding from aortic rupture is usually internal, into pericardial sac, pleural cavity mediastinum, or other great vessels (pulmonary artery innominate artery superior vena cava, innominate vein) infrequently it is external into esophagus trachea, bronchus, or through the skin when the aneurysm has perforated the bony chest wall.

Spontaneous rupture of the diseased or weak aorta most often occurs during unusual exertion, but it may take place at rest commonest is the rupture of a saccular aneurysm, almost always syphilitic next most common is complete or almost complete transverse rupture a little above the aortic valve; then there are tears in the inner and outer coats not immediately opposite each other and finally there are the dissecting aneurysms (Harris, 1938) Occasionally there are incomplete aortic wall tears that are an accidental finding at autopsy (Perry 1942)

Simple diffuse dilatation of the aorta mainly of the ascending portion and arch, common in chronic hypertension and aortic regurgitation, is, as a rule, unimportant, since the aortic wall may be otherwise normal with good muscle and elasticity if however there is in addition atherosclerosis, medial necrosis, or aortitis, the hypertension or aortic regurgitation may be an important extra burden favoring the production of aneurysms and rupture. Extreme ectasia is rare.

Effect of aortic disease on the heart The heart itself may or may not show signs of involvement in the presence of disease of the aorta such involvement is either incidental, due to coronary artery disease, hypertension, or valvular disease, or it results from complications of the aortic disease such as syphilitic aortic regurgitation, narrowing of the mouths of the coronary arteries, or arteriovenous aneurysm by rupture of aorta into a great vein. Left ventricular enlargement is the chief finding in such cases.

Uncomplicated aortic disease does not cause any demonstrable change in the heart either functionally or pathologically

Symptoms. There are no definite symptoms of aortic disease except those which result from the most common complications (1) distress due to pressure from aneurysmal dilatations, (2) excruciating pain from tearing of the aortic wall in the case of dissecting aneurysms, and (3) angina pectoris or pain elsewhere in the body caused by occlusion of the mouths of the coronary or other arterial branches. Rare cases with slow bleeding from rupture may also have symptoms hemoptysis, hematemesis, weakness, pallor Involvement of the wall itself without aneurysmal pressure, medial dissection, or arterial mouth occlusion has been blamed as a cause of symptoms, especially of pain, often of the nature of angina pectoris, but there is no proof that simple aortic wall involvement can cause pain, it is now quite certain that angina pectoris is a symptom of coronary insufficiency whether or not the result of narrowing or occlusion of the coronary mouths, rather than that it is a symptom of aortic disease alone. Usually there are no symptoms at all from disease of the aorta.

Signs. As in the case of symptoms, so in the case of signs, there is no evidence of slight structural disease of the aorta. Extensive involvement, often of syphilitic nature, produces signs mostly dependent on dilatation of the aorta (Figure 143 over) Dilatation due to hypertension may also be visible by roentgen ray examination (Figure 96, page 476) Atherosclerosis, if extensive, results in an elongation and tortuosity of the aorta due to loss of elasticity this tortuosity with prominence of the aortic knob (uppermost curve of the arch to the left) evident by roentgen ray study is a very common finding in old age (Figure 144 page 749) Advanced atherosclerotic changes with calcification in the aortic wall make the roentgen ray shadow of the aorta more dense than normal.

Roentgenology continues to be the most important means of detection of aortic disease, for it is only when dilatation of the ascending aorta or arch has reached a high degree that it becomes evident on ordinary physical examination—inspection, palpation, percussion, and auscultation. As a matter of

fact even roentgenology itself is a crude method of diagnosis, deformity or calcification of the aorta being necessary before the roentgen ray picture appears abnormal. Frequently fluoroscopy shows greater dilatation of the aorta than is found at postmortem examination because of the dynamic dilatation present during life, under high intra-aortic pressure. Marked aortic

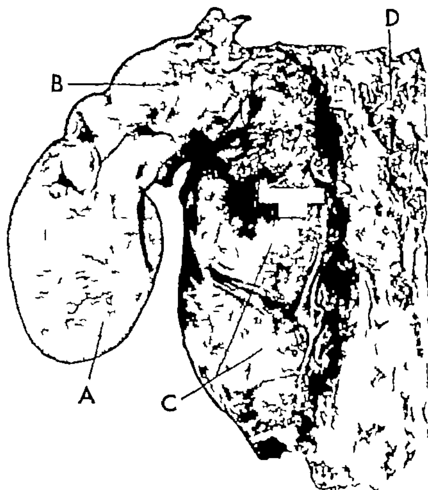


FIG. 143 Syphilitic aorta with large aneurysm of the descending thoracic portion compressing and eroding the vertebrae and spinal cord with resulting paraplegia. (A) Heart, (B) arch of aorta, (C) aneurysmal sac, and (D) vertebral column. (Kindness of Dr Pedro Castillo, Havana, Cuba.)

pulsation is often visible fluoroscopically with marked aortic regurgitation, especially when the heart action is very forceful. Occasionally large or thick aortic plaques (calcification) are apparent on roentgen ray examination. Finally it is important that roentgenologic examination should include the oblique views as well as the anteroposterior view because the shadow of the great vessels sometimes appears very wide in the anteroposterior view when



FIG. 144. Roentgenograms showing dense sclerotic aorta throughout its course in the thorax. The heart is slightly displaced to the right by the high level of the diaphragm on the left. The aortic notch in the barium-filled esophagus is clearly visible at the beginning of the aortic arch. (*A*) Anteroposterior view (*B*) left anterior oblique view

the aorta is simply kinked or tortuous and not dilated. Erroneous diagnoses of dilatation and even of aneurysm have sometimes been made by hasty roentgen ray study. In obscure cases roentgen films taken after the intravenous or, more usefully still, arterial or direct aortic injection of contrast fluid may give the necessary information.

Dilatation of the aorta is usually accompanied by a systolic murmur more or less localized, in the second intercostal space just to the right of the sternum, varying in intensity and in extent of transmission, but less intense and not so widely transmitted as is the systolic murmur of aortic stenosis. The most important points of differentiation between aortic dilatation and aortic stenosis are the obvious aortic enlargement by roentgen ray study in the former and the palpable systolic thrill, decrease or absence of the aortic second sound, and decrease of pulse pressure, often with plateau pulse, in the latter. Lesser grades of aortic stenosis are difficult or impossible to diagnose, especially if there happens to be coincident aortic dilatation. Dilatation of the aorta may be accompanied by signs of aortic regurgitation, commonly organic and often due to syphilis but of functional nature in some cases. marked rheumatic aortic regurgitation may result in aortic dilatation, which is well shown by roentgen ray.

Enlargement of the left ventricle, as evidenced by physical examination, roentgen ray study, and electrocardiography (abnormal left axis deviation), follows aortic regurgitation complicating aortic disease, while myocardial malnutrition, scattered fibrosis, and even infarction may follow narrowing of the coronary mouths, producing the usual signs, such as abnormalities of the electrocardiogram, already described (Chapter 21). Heart failure of congestive type may succeed either of the two complications of disease of the aorta which especially affect the heart, namely, aortic regurgitation and coronary mouth occlusion, but especially the former. Slight to moderate degrees of acquired aortic disease usually produce no signs of cardiac involvement.

Signs due to aortic aneurysms will be discussed later in this chapter.

Course and prognosis. The course and prognosis of aortic disease depend on two conditions, the etiologic factor and the degree of involvement. Usually atherosclerosis is a slow process continuing to old age. It is not in itself a serious condition except in very rare instances of aortic wall rupture or of intra-aortic thrombosis over an eroding or brittle plaque. Extensive atheroma is, however, an unfavorable omen for very long life since it exists more often in persons who die under the age of seventy-five than in those who survive that age. Infectious aortitis may not be serious but it often is. Acute or subacute bacterial endarteritis, like acute or subacute bacterial endocarditis with which it may be associated, is now curable by the administration of penicillin or other specific remedy in the course of weeks or months, while syphilitic aortitis which used to limit life to an average duration of about three years after its discovery now permits a good many long survivors when the newer measures of treatment are carried out (see Chapter 16). In the severer cases of rheumatic infection and typhoid fever aortic lesions may develop.

Rupture of the aorta as a rule is rapidly fatal, but rare cases have existed in which the rupture was small or the bleeding gradual, and even spontaneous repair has been noted.

Aneurysms, saccular or dissecting, are serious, the former permitting as a rule but a few months to a few years of life after their discovery and the latter generally fatal in the course of a few hours, days, or weeks. Infrequently a dissecting aneurysm allows survival for a few months or years with double aortic channel.

Complications. Important complications of disease of the aorta, varying with the cause, consist in the main of (1) cardiac enlargement and failure which may or may not be secondary to the aortic disease, (2) aneurysmal formation, and (3) rupture of the aortic wall. The first and last of these complications have been discussed above; aortic aneurysms will be discussed later in this chapter.

Disturbance of the cardiac rhythm in aortic disease is unusual.

Treatment. The treatment of aortic disease varies with its cause and degree, and with the type and extent of complications. It is discussed separately under cardiovascular syphilis (Chapter 16), bacterial endocarditis (Chapter 15), congestive heart failure (Chapter 30), and aneurysm (the present chapter). There is no effective treatment as yet for atherosclerosis, but avoidance of overexertion and overeating, and protection against infection are advisable. For a great many years potassium iodide has been given empirically in the treatment of arteriosclerosis; there is a possibility, but no real proof as yet, that this drug may have some influence in retarding the development of this process in man. Choline and other lipotropic agents are now being tested in order to determine their therapeutic and prophylactic action in human atherosclerosis.

Differential diagnosis. The chief difficulty in the differential diagnosis of a diseased aorta comes in distinguishing it from a normal aorta, since in a large majority of cases of atherosclerosis and inflammation there are no symptoms or signs, and when there are such symptoms and signs they are often so slight or obscure that a clear diagnosis is impossible. When aortic dilatation or other abnormalities are well marked they must be differentiated from mediastinal disease and tumors, and from heart disease of other nature than that associated primarily with aortic disease. Often the differentiation is difficult and in a large number of cases aortic disease is complicated by factors like hypertension, coronary disease, or valvular disease which obscure the primary aortic abnormalities.

CONGENITAL AORTIC DEFECTS

Congenital aortic anomalies, found mostly in young persons, are due to maldevelopment in fetal life or at birth and include hypoplasia, coarctation, right aortic arch, double aortic arch, vascular rings involving aorta—especially double aortic arch and major branches of aorta (in particular the right sub-

clavian) and transposition of the aorta and pulmonary artery septal defects between aorta and pulmonary artery right ventricle, or atrium, and patency of the ductus arteriosus these defects are discussed in Chapter 13

DISEASES OF THE PULMONARY ARTERY

The pulmonary artery is subject to nearly all the diseases and abnormalities that affect the aorta but in less frequency and degree. Nevertheless, cases exist in which this artery and its branches are involved to a considerable extent, and it has been shown in recent years that structural changes in the smaller pulmonary vessels are extremely common and sometimes play a role in the precipitation or exaggeration of circulatory trouble (Costa, 1927 Brenner 1935)

An important new method of studying the pulmonary circulation, with particular reference to its blood pressure, has been introduced in the last few years and has already clarified some hitherto unsolved problems; the method consists in the catheterization of the pulmonary artery and its branches via the heart (see Chapter 10)

From a careful study of a series of 100 consecutive unselected autopsied cases at the Massachusetts General Hospital, Brenner drew the following conclusions "This lengthy survey seems to show that the pulmonary circulation plays an important part both in the physiology and in the pathology of the circulation as a whole, but that this part is, with rare exceptions, passive rather than active. The structure of the pulmonary vessels is such that they cannot be expected to play an important part in the regulation of the circulation through the lungs By far the most important influence in regulating the pulmonary circulation is the activity of the heart and particularly the state of balance between the two sides of the heart, an increased output of the right side or a diminished output of the left causing congestion of the lungs and vice versa. Again, the pulmonary circulation has so great a reserve (provided by the ready distensibility of the small pulmonary vessels and the large number of 'reserve capillaries through which blood does not ordinarily flow) that it is difficult to embarrass it by occluding large branches of the pulmonary artery The cross-sectioned area of the stem of the pulmonary artery must be diminished by 75 per cent before the systemic blood pressure falls and by 90 per cent before death occurs (in acute experiments)

Practically all the varieties of vascular disease occurring in the systemic circulation may be observed also in the pulmonary circulation. Some forms, such as syphilitic arteritis, are less common, and others, such as septic and tuberculous arteritis, are more common than in the systemic circulation. Atherosclerosis is exceedingly common, having been noted microscopically to some degree in 97 per cent of 100 consecutive unselected autopsies. Its incidence is therefore as great, though its degree is not so marked, as in the systemic circulation. Its very frequency makes it difficult to determine etiologic factors, though its severity increases somewhat with age and with conditions

thought to be associated with a raised pulmonary arterial pressure, such as cardiac disease or chronic pulmonary disease. No constant relationship is found between the thickness of the right ventricle and the degree of pulmonary atherosclerosis.

"Thrombi, whether embolic or formed in situ, are common in the pulmonary circulation, being found in 28 of 100 consecutive unselected autopsies. They ultimately become completely organized. They rarely cause symptoms unless a large branch of the pulmonary artery is suddenly blocked."

Etiology and pathology The commonest lesion of the pulmonary artery wall is *atherosclerosis* which is found particularly in cases of chronic mitral valve disease and chronic lung disease (especially extensive fibrosis) Such atheroma has been attributed to the increased strain on the artery and its branches by the hypertension in the pulmonary circulation. In some cases pulmonary atherosclerosis exists without any lesion elsewhere. There is apparently but little relationship between sclerotic changes in the aorta and in the pulmonary artery The pulmonary arterial atherosclerosis is usually slight, consisting simply of yellowish fatty areas (atheroma) without calcification plaques which are so frequent in the aorta are unusual in the pulmonary artery Atherosclerosis of this artery is thus of little or no significance in most cases it is simply a pathologic finding of academic interest.

Infection of the pulmonary artery is occasionally found in slight degree, especially in rheumatic infection or bacterial endocarditis. Syphilitic involvement either of the main artery or of its smaller branches is very rare, but it may be responsible for aneurysm or thrombosis of some part of the pulmonary arterial circulation.

Endarteritis obliterans of the smaller pulmonary arteries, which is a rare but serious and generally rapidly fatal condition, has been attributed in some cases to syphilis, but as a rule it is of unknown cause.

Congenital defects include communications between pulmonary artery and aorta, and transposition of these great vessels these have been discussed in Chapter 13 There is also hypoplasia, associated at times with congenital pulmonary stenosis. Congenital dilatation is occasionally seen with patency of the ductus arteriosus, with interatrial septal defects, and even with pulmonary stenosis. Aneurysmal dilatation due to weakness of the wall may also occur but much more rarely

Trauma is infrequent as a cause of pulmonary artery disease, but rupture and traumatic aneurysm of the main trunk and of the branches have been noted, as in gunshot wounds.

One of the most serious of all affections of the pulmonary circulation is that of obstruction by *thrombosis* or *embolism* most commonly the latter Thrombosis is the result of a primary pulmonary artery lesion—endarteritis of inflammatory or obliterans nature—or perhaps of chronic stasis, except when it occurs secondary to obstruction by embolism. Embolism is a sudden invasion of a generally normal pulmonary arterial tree by a clot from a thrombosed vein somewhere in the body (in the great majority of cases from legs,

pelvis, or abdomen)—this will be discussed in more detail in the next section of this chapter

Hypertrophy of the smaller pulmonary arteries with increased thickness of their walls, is a common result of chronic pulmonary hypertension from any cause, especially in younger patients.

Finally *dilatation of the pulmonary artery* and its main branches without lesions of the wall, except occasionally atheroma, is a fairly common acquired finding with hypertension of the pulmonary circulation in mitral stenosis, congenital atrial septal defects, extensive blocking of the pulmonary circulation, or advanced disease of the lungs. Some of this dilatation is permanent, but some is temporary due evidently to the dynamic effect of the increased blood pressure and acutely caused by massive pulmonary embolism before the circulation and the right ventricle fail. Rarely pulmonary artery dilatation is congenital. Regurgitation through the pulmonary valve may or may not be found in cases of pulmonary artery dilatation.

The pathologic characteristics of the various lesions mentioned above are the same in nature but as a rule much less in degree than those described under aortic disease.

Symptoms. There are no symptoms of pulmonary artery disease itself, except those associated with sudden occlusion of a large part of the pulmonary circulation by embolism, with extensive obstruction of the smaller branches, or with right heart failure In the case of massive pulmonary embolism there are at first usually air hunger and collapse, and sometimes anterior chest oppression later fever cough, hemoptysis and localized chest pain (due to infarction) usually develop if the patient survives the initial catastrophe. With extensive obstruction of the smaller pulmonary vessels there are dyspnea and cyanosis. When the right heart fails liver engorgement and dependent edema develop

Signs. Signs of pulmonary artery disease are few In fact, there are no signs at all unless there is dilatation of the main trunk and its major branches, the presence of which may be shown by physical examination but much better by roentgen ray study or unless there is obstruction, due to chronic endarteritis, thrombosis, or embolism, when cyanosis and right heart failure may be marked. The cyanosis, due to the greatly limited area of pulmonary capillary surface exposed to the inspired air may be intense in rare cases, especially in those with endarteritis to whom the term "black cardiacs" has been applied. Physical signs of pulmonary artery dilatation include a loud pulmonary systolic murmur accentuated pulmonary second sound, increased percussion dullness at the left upper cardiac border and sometimes visible and palpable pulsation over the pulmonary artery A state of serious shock, often fatal, with very low arterial and venous blood pressures may supervene when there is sudden and considerable pulmonary obstruction due to embolism from peripheral venous thrombosis which occasionally occurs as a postoperative complication or even more commonly in the course of chronic heart disease.

Frequently associated with abnormality of the pulmonary artery is right ventricular enlargement, revealed by various methods of study; there is left atrial enlargement only when the left ventricle has failed or mitral valve disease is present. With considerable dilatation of the pulmonary artery the valve ring may become incompetent and the murmur of pulmonary regurgitation may then be evident.

Signs of infection underlying lesions of the pulmonary artery are of course incidental and do not aid materially in the diagnosis except in determining the type, as in the case of syphilis or acute bacterial endocarditis.

Course and prognosis. The course and prognosis of pulmonary artery lesions vary greatly. Usually they are entirely favorable but in the case of extensive pulmonary endarteritis obliterans the structural defect itself may prove fatal in the course of a few months or years; in the case of chronic stasis of high degree in the pulmonary circulation thrombosis and infarction may be superimposed on serious heart disease as an insuperable burden; and in the case of pulmonary embolism death may result in a few minutes, hours, or days, or recovery follow after a more or less stormy illness. As a rule pulmonary artery disease is a postmortem finding, not diagnosed or diagnosable during life.

Complications. Complications consist chiefly in enlargement and failure of the right ventricle. There may or may not be other cardiovascular lesions present. Heart disease, especially mitral stenosis and left ventricular failure, are common. Pulmonary arterial aneurysms and rupture are very rare.

Treatment. The treatment is that of the underlying disease or complication. In the case of obstruction due to endarteritis, thrombosis, or embolism, oxygen therapy should be employed to reduce cyanosis and dyspnea. Operative removal of pulmonary emboli has been successfully accomplished (first successful case reported by Kirshner in 1924) and frequently advised in the past but only rarely has it been attempted, because it is excessively difficult to select the proper case and time for such a radical operation, it seems very unlikely from the experience of the last twenty years that such embolectomy will ever prove feasible. Preventive measures, however, have already proved their worth. If it is evident, for example, that pulmonary embolism has resulted from peripheral phlebothrombosis, the leg veins should be ligated to prevent recurrence and for prophylaxis anticoagulant therapy is in order.

Differential diagnosis. The diagnosis of pulmonary artery disease is often impossible; only with well-marked changes is it more than a guess. Differentiation from pulmonary valve lesions may be very difficult; the presence of mitral stenosis, of chronic failure of the left ventricle, of chronic pulmonary fibrosis, of recent operation or accident (which would favor pulmonary embolism) and of pulmonary artery dilatation are the distinctive points which aid in the diagnosis of involvement of the pulmonary artery. Cardiac catheterization to determine the pulmonary arterial pressure is occasionally a helpful procedure. The differential diagnosis between pulmonary embolism and acute coronary occlusion is sometimes especially difficult, for that purpose seria-

electrocardiography is of particular value (see Chapters 20 and 21 and the next section)

PULMONARY EMBOLISM

In the first two editions of this book pulmonary embolism one of the most important of all cardiovascular disorders, was seriously neglected, but this omission was largely corrected by the addition in the third edition of ten pages about this subject. In the present edition references to new advances have been added.

It is an astonishing and disconcerting fact that I and many others had been examining and treating patients for years without realizing what we know now namely that pulmonary embolism, instead of being predominantly a surgical, or rather postoperative, complication is actually much more commonly a condition occurring in the practice of internal medicine, particularly in heart disease itself Until recently it has been called all sorts of things, uncommonly recognized during life for what it actually was. It has not suddenly appeared out of the blue a new disease in its frequency we have merely at last become aware of it.

Its great importance lies not so much in its frequency but rather in its serious significance and in its preventability It belongs in some detail in this book not only because it is a cardiovascular event of much importance, but because, like dissection of the aortic wall, it involves the great vessels and is an intrathoracic disease that may simulate or complicate heart disease itself, in contrast to the various peripheral vascular lesions, and especially because in its protean manifestations and details it is not adequately presented in most of the medical literature, even of the present day

Incidence Pulmonary embolism is variously recorded as being found in 8 to 12 per cent of routine autopsies, in 5 to 10 per cent of postoperative deaths, in 0 1 to 0.5 per cent of all cases operated upon, and sooner or later in a large percentage of cardiac patients (31 per cent of autopsied cases of mitral stenosis and 48 per cent of autopsied cases of congestive heart failure—Levine and White, 1937 and Kinsey and White, 1940 respectively) In one autopsy series 60 per cent of the cases were medical (half of which were cardiac) and 40 per cent were surgical (Hampton and Castleman, 1940) of another series of 247 cases 166 were medical, 80 postoperative or posttraumatic, and one occurred postpartum (Westdahl, 1941) In a recent survey of cases at the Massachusetts General Hospital, there were 273 cases (0.6 per cent) among 45,523 medical patients and 238 cases (0 24 per cent) among 98 642 surgical patients during the years 1936 to 1945 inclusive (Carlotti, et al., 1947) In my own cardiovascular practice the recognized incidence jumped from 0 4 per cent in the decade 1920 to 1930 up to 3 0 per cent in the decade 1930 to 1940, due in all probability to better acquaintance with the condition (White, 1940) Even the pathologist and the roentgenologist with their accurate methods of study realize their large oversight of pulmonary em-

bolism in the past (Hampton and Castleman, 1940) After World War I the German medical writers commented on the increased postwar frequency of pulmonary embolism (Burwinkel, 1928) which was variously attributed to poor physical condition and malnutrition, to the increase of surgery and, because of the advance of surgery to the subjection of more older persons to operations though these factors were quite possibly operative, it seems likely that the recognition of the condition was also keener Erdheim the great pathologist of Vienna, had been one of the few who was early cognizant of the true situation.

Etiology *Cause* The one outstanding cause of pulmonary embolism is *phlebothrombosis of the leg veins* beginning as a rule in the calf and extending into the long saphenous and femoral veins in one or both legs. The thrombus is usually bland and dependent on stasis in a local circulation that has already been defective either structurally or functionally It is not infective or based on infection and so the term phlebothrombosis is preferable to thrombophlebitis Other veins in the body pelvic, abdominal, brachial, and thoracic, are much less likely to be responsible even though they may be at or near the site of operation or injury that has occasioned the rest in bed. Nor are the right heart chambers often the locus of origin of the clots special exceptions should be made in the case of bacterial endocarditis involving a congenitally deformed right heart chamber or valve or patent ductus arteriosus, and myocardial infarction of the interventricular septum with resulting thrombus formation on the injured myocardium.

The leg phlebothrombosis occurs with equal readiness in the medical and in the surgical or traumatic cases predisposed by the circulatory stasis occurring in chronic or acute illness as from heart disease with congestive failure, myocardial infarction, cancer abdominal and pelvic operations, and serious accidents. Excessive manipulation of the abdominal or pelvic viscera at the time of operation and a long-sustained Trendelenburg position favor the leg vein stasis. Sitting still for hours with the knees bent favors the occurrence of thrombosis in the leg veins in an older person.

Exciting factors. In the majority of cases the embolus breaks loose without any particular provocation, but sometimes some strain is responsible, especially administration of an enema or use of a bedpan.

Age Pulmonary embolism occurs postoperatively much more commonly in older persons but is fairly frequent as a complication of heart failure in middle-aged or young adults It is rare before the age of twenty

Sex The sexes are fairly evenly represented.

Pathology The structural changes concerned with pulmonary embolism are three (1) the clot in the leg vein which becomes the embolus, (2) the actual plugging of one or more of the pulmonary arteries by that clot, and (3) the pulmonary infarct that may follow Each one has its signs and symptoms. The first two conditions always occur but not the third

The clot itself is a very rapidly propagating thrombus loosely attached to the wall of the leg vein and often floating in the blood stream ready to break loose

at any moment. If in the course of its evolution this clot becomes well fixed it then loses its threat and in time becomes organized in situ, doubtless that frequently happens and we never know how often patients escape further trouble. By the time a clot becomes solid and, by obstructing a vein, produces signs and symptoms, that particular clot has lost its embolic tendency although a sister or daughter clot may still get loose. Thus in phlebothrombosis the pulmonary embolus may come from the leg that seems normal, the other leg being swollen and sore as the result of the venous obstruction which has revealed the underlying disease It is the lengthy clot from the long saphenous or femoral vein that is especially dangerous and that, coiled up, may massively block the main pulmonary artery

The actual *blockade of blood flow* in the pulmonary circulation varies tremendously in degree and location, from almost complete obstruction of the main pulmonary artery to closure of a small branch on either side the former kills quickly the latter in an otherwise healthy person probably produces no symptoms or signs at all. Rarely is the embolus a septic one or composed of tumor cells, or in the dog made up of the long worms of Dirofilaria immitis. The left lower lobe has been the most common location of embolism or infarction at the Massachusetts General Hospital, but both lower lobes are frequently involved together during the years 1937 to 1943 the location of 171 pulmonary emboli at the Massachusetts General Hospital has been as follows. left lower lobe 99 (57 9 per cent) right lower lobe 65 (38 0 per cent) right upper lobe 4 (2.3 per cent) right middle lobe 0 and left upper lobe 3 (1.8 per cent) Pulmonary embolism is often, perhaps usually multiple sometimes as many as one to two dozen emboli enter the lungs in the course of a few days or weeks, varying in size from small fragments of clot to thrombi a foot or more long which may cause rapid death.

Pulmonary infarction is by no means a necessary sequel of pulmonary embolism, being found in only about half of the recognized cases of pulmonary embolism. The pulmonary circulation is so rich in anastomotic and collateral connections that infarction results only if the occlusion is large or the area of one of the lobes is involved or some obstruction to the blood flow is already present, as in congestive failure of the left ventricle or in mitral stenosis. The infarction may be partial and temporary yielding no signs and leaving no scar or it may be complete, with ample signs and scar formation. Thus it is obviously important not to use the terms pulmonary embolism and pulmonary infarction synonymously

Symptoms. The symptoms of pulmonary embolism vary from none to many from mild to overwhelming. The commonest is the sudden onset of *dyspnea* not attributable to effort or excitement or to abrupt heart failure from paroxysmal tachycardia in a cardiac patient. Rarely an asthmatic type of breathing is set off A symptom that is a close second is *substernal oppressive pain* which often accompanies the dyspnea and in older patients with limited coronary reserve may include or actually consist entirely of angina pectoris due to the effect of anoxemia or of the strain of the event on coronary heart

disease already present, on occasion the pain may predominate. A *feeling of faintness* is common, while a *state of shock* is not at all rare, being found naturally in the more severe cases or in patients already quite ill before the pulmonary embolism occurs. *Restlessness* and *sweating* are often seen as a part of the reaction to the embolism. Other symptoms are uncommon: nausea and vomiting, cough, chill, and headache. Sometimes a mere sense of uneasiness or malaise reveals the occurrence of a small embolus.

Fever develops if there is an infarct in the lung, but there may already be a slight febrile reaction to the underlying phlebothrombosis in the leg. With a large infarct the temperature may rise to 103° or 104° F by mouth. Fever of a degree or two that occasionally accompanies congestive failure is more often due to *pulmonary infarction than to any other cause; it has been in the past* wrongly ascribed to pulmonary infection which may, to be sure, occur (but less commonly) or to the congestive heart failure itself.

Pleural pain on the affected side is a common complication if there is an infarct, becoming evident on respiration on the second day and continuing for a few days, with or without a pleural friction rub.

Blood spitting is important evidence in favor of the diagnosis if it occurs, but it is actually relatively uncommon. It is often in larger amounts than in the case of pneumonia and does not resemble the frothy pink sputum of the pulmonary edema of acute left ventricular failure. Most cases of congestive heart failure do not raise any blood at all.

Signs. The two most important signs of the acute process and for a while afterward are *cyanosis* and *tachycardia*, out of all proportion to any evidence of heart failure, pneumonia, or fever. The cyanosis is frequently of high degree and is the occasion for rushing oxygen to the patient. The tachycardia on occasion is of paroxysmal nature, atrial ectopic, or atrial fibrillation, or atrial flutter, and this abnormal rhythm may divert one's attention from the underlying lesion. As a rule, however, the tachycardia, often as fast as 140 to 160, is sinus in origin, the patient may himself become aware of the fast pulse but usually he is more troubled by other things, particularly the dyspnea and prostration.

Jaundice is a rare but important sign of a large pulmonary infarct superimposed on a liver congested from heart failure and unable to cope with the excess of blood pigment.

Localizing signs, either of the *phlebothrombosis in the leg* (tenderness, swelling, pain on flexion of the foot—Homan's sign) or of the *involvement of the lung* (local râles, bronchial breathing, pleural friction rub or fluid) are often conspicuous by their absence. They should be looked for daily; when found they aid greatly in the diagnosis.

Laboratory data. Information derived from laboratory study is usually less important than the symptoms and signs already presented; sometimes it is helpful in confirming or even pointing to the correct diagnosis, but at other times it is misleading because it shows so little or because it reveals unexpected findings.

Roentgen ray examination. At the onset and for 24 hours or more afterward there may be little to find wrong in the thorax by roentgen ray even with developing infarction of the lung, except for elevation of the diaphragm on the affected side or distended main pulmonary trunks with decreased caliber of vessels below helpful signs which should be looked for If there is no infarction roentgen ray evidence may be lacking, but sizable infarcts finally appear in the picture as shadows of any shape and size at the periphery of either lung, often tucked away in the sharp costophrenic angles where they may be mistaken for fluid. Besides the two difficulties with roentgen ray diagnosis of pulmonary embolism already mentioned, namely the slow development of the evidence when such finally appears and its complete absence when there are no infarcts, there is one other problem that is often insuperable, namely that the shadow of an infarct may be hidden by the hydrothorax or pulmonary congestion due to underlying heart failure, by pleural fluid resulting from the infarct itself or by the heart shadow which is so often enlarged in these cases.

Multiple shadows may appear in the lungs on the roentgen ray films due to recurrent emboli with infarcts and be mistaken for areas of bronchopneumonia or tumors (Figure 145A) and in recent years linear scars of pulmonary infarcts have been identified by pathologist and roentgenologist (Hampton and Castleman, 1940) so that it is possible on occasion to unravel past episodes of pulmonary embolism (Figure 145B) Indeed sometimes old scars and fresh infarcts are present in the same case.

In pulmonary embolism it is even more important to investigate the venous circulation in the leg than it is to study the lungs, inasmuch as the threat to further trouble which may be fatal lies in the femoral veins. Physical examination may quickly reveal the thrombosis by the discovery of tenderness, swelling, or recently discolored skin, and then roentgen rays are unnecessary but often (in over 50 per cent of the cases) there are no signs of the thrombosis. One may of course, assume that it exists none the less and go ahead with the ligation of the leg veins on both sides without more ado. Some years ago it was the custom in various clinics for roentgenologic diagnostic purposes to inject some contrast medium (e.g., Diodrast) into the veins of the lower leg when thrombosis therein was suspected, but this procedure has been in large part abandoned for two reasons (1) the veins, even though not thrombosed, were not always adequately filled, and (2) on occasion thrombosis was actually precipitated or aggravated by the material injected.

Electrocardiography In the majority of cases of pulmonary embolism the electrocardiogram is of no assistance. A few cases, about 10 per cent, with severe enough pulmonary arterial obstruction to cause the acute cor pulmonale, but without severe shock, have electrocardiograms with characteristic pattern of dilatation of the right ventricle, consisting of prominence of *S* waves in Lead 1 and in the precordial leads over the left ventricle, of *Q* waves in Lead 3 low to slightly inverted *T* waves in Lead 2, inverted *T* waves in Lead 3 and in the precordial leads over the right ventricle (Leads V_1, V_2, and sometimes V) (McGinn and White, 1935 Murnaghan, McGinn, and White, 1943) (See Figure 99 and Chapter 20)



FIG. 145 Roentgenograms showing (*A*) fresh pulmonary infarcts of lower lobe of right lung (kindness of Dr Richard Schatzki, Mt. Auburn Hospital, Cambridge) and (*B*) clearing infarct upper portion of right lower lobe (kindness of Dr M. C. Sosman, Peter Bent Brigham Hospital, Boston) (*C*) ( ) 12 days before and (*b*) one day after the occurrence of postoperative pulmonary embolism. Note in *b* the thrombosed pulmonary arteries consisting of rounded shadows at the hilus regions in contrast to *a*, and the decreased vascular markings below the hilus shadow on the right resulting from the decreased blood flow there.

Besides the relatively small number of cases of pulmonary embolism showing the acute cor pulmonale pattern of electrocardiogram, there are three other groups, the largest of which, because either of the small size of the embolus or at least of its failure to disturb the heart appreciably shows no change in the record from the normal or abnormal findings prior to the embolism. Another fair sized group consisting of older persons with limited coronary reserve and often already afflicted by coronary heart disease, may develop under the strain of the pulmonary embolism itself or of the vascular shock that accompanies it sufficient myocardial ischemia and anoxemia to produce coronary types of electrocardiograms (see Chapter 21) or indeed even acute myocardial infarction itself (posterior or anterior) without actual acute coronary thrombosis. Finally severe depression of the coronary circulation with anoxemia in high degrees of pulmonary artery obstruction or vascular shock may itself cause temporary changes in the electrocardiogram which may simulate coronary heart disease though none has been present previously or will result after recovery

Thus, it is apparent that the electrocardiographic findings in pulmonary embolism can be entirely normal, quite characteristic of one pattern or another or very complicated due to a combination of several effects (Murnaghan, McGinn, and White, 1943)

Other data Other laboratory findings in pulmonary embolism are unimportant. Leukocytosis of slight to moderate (rarely high) degree is found when there is pulmonary infarction, which explains the blood picture as it does the fever in many cases of congestive heart failure. Examination of blood, sputum urine, and chest fluid shows nothing of special interest.

Course and prognosis. Pulmonary embolism may kill quickly though not instantaneously but more often there is recovery Of one group of 70 fatal cases, 6 died in less than ten minutes and 16 more within an hour of the remaining 48 cases, 20 died within twelve hours, 4 between twelve and twenty-four hours, and 24 lived for one to several days (de Takats, 1940) Of the cases that recover many have recurrent embolism In de Takats series of 100 cases 39 per cent suffered a second attack, 12 per cent had a third, 5 per cent a fourth, 3 per cent a fifth, and 1 per cent a sixth. Doubtless the embolism is often so slight that it escapes notice altogether

This common recurrence of pulmonary embolism is one of its chief diagnostic features setting it apart from the two conditions with which it is so often clinically confused, namely myocardial infarction and pneumonia which do not so rapidly recur daily or weekly Perhaps a patient does have acute coronary occlusion or pneumonia to start with, but when some sort of acute trouble in the chest keeps repeating itself every few days one should not only think at once of pulmonary embolism but also suspect that even the first attack of all may have been that very condition.

Pulmonary embolism may occur as early as the first day after operation or accident or it may not happen till after three months in a large series of cases (897) at the Mayo Clinic approximately one half occurred between the

seventh and fourteenth days, one quarter during the first seven days, and one quarter after the fourteenth day (Barker et al., 1941) The intervals between first and second episodes, or between first and last (if more than two) in 207 cases of recurrent embolism in the Mayo Clinic Series was less than a day in 27 per cent, between 1 and 7 days in 38 per cent more, and less than 10 days in about four fifths of the cases. In recurrent embolism the attacks vary greatly in severity from very mild to fatal thus, the symptoms and signs will vary accordingly If the first attack or two have been severe, however a succeeding slight attack may be enough to kill the patient or at least to cause symptoms and signs out of all proportion to the actual size of the embolus. Likewise if serious heart or other disease is already present the very first pulmonary embolus, even though small, may precipitate congestive failure or myocardial infarction or be the cause of death in fact the commonest last straw which terminates life in patients with heart disease is pulmonary embolism.

The mortality from recognized pulmonary embolism is variously estimated as 20 to 40 per cent but doubtless this figure is too high, small emboli remaining undiagnosed. Nevertheless it remains one of the most fatal of diseases.

Recovered cases of pulmonary embolism may show no sequelae whatsoever or they may bear the linear scars of the pulmonary infarcts, identified by roentgen ray and autopsy Such scars are as a rule entirely unimportant. Rare cases, however of massive pulmonary embolism recover to develop slowly the chronic cor pulmonale (doubtless having suffered originally from the acute cor pulmonale) The large clot in the pulmonary artery or its main branches becomes organized and the marked pulmonary hypertension gradually enlarges the right ventricle so that in the course of a few months or years death may come with right heart failure, with or without recurrent pulmonary embolism from recurrent phlebothrombosis or pulmonary thrombosis in situ superimposed on the old organized embolus.

Complications. The commonest complication of pulmonary embolism is pulmonary infarction already described. Attending such infarction there may be pleuritis and pleural effusion or a secondary infection of bronchopneumonia. Acute vascular shock is an occasional and very serious complication. Another reaction which has been described is that of bronchial and perhaps coronary spasm secondary to the vagal reflex set off by the event; the frequency degree, and importance of this have not been demonstrated. In a minority of cases, probably about 10 per cent, there is an important degree of dilatation of the right ventricle (the acute cor pulmonale—see Chapter 20) In the presence of heart disease the serious complications of congestive heart failure and myocardial infarction may be further complicated by pulmonary embolism, which, vice versa, in its turn may precipitate either congestive failure or myocardial infarction.

Treatment. The lesser degrees of pulmonary embolism may require no treatment per se but cases of severe grade with dyspnea, oppressive pain, cyanosis, and tachycardia, with or without the acute cor pulmonale or shock, need emer

gency treatment consisting of opiate (e g. morphine sulphate ¼ gr [0 015 gm] subcutaneously) oxygen (by tent or Boothby mask in high concentration, preferably 100 per cent) and expert nursing care. The first few hours are the critical ones.

Other therapy is less important but may be helpful. Atropine sulphate 1/100 to 1/60 gr (0 0006 to 0 001 gm) and also papaverine hydrochloride ½ gr (0 03 gm) have been advised subcutaneously or even intravenously for rapid effect in the syncopal type of pulmonary embolism, as antispasmodics, but their routine general value has not been proved. Also digitalis solution (equivalent to 0 3 gm or 4 ½ gr of the international standard strength) or strophanthin (1/120 gr or ½ mg) has been advised to be given intravenously for the acute cor pulmonale but the effectiveness of these drugs also remains to be demonstrated.

Otherwise only symptomatic treatment is indicated except for two important measures. If the diagnosis is clear either the leg veins should be ligated at once, or the anticoagulant heparin be given by vein, or Dicumarol begun by mouth, to maintain a clotting time of ½ to 1 hour The leg veins should be investigated, the offending veins (commonly the superficial femorals) being ligated, preferably on both sides, to prevent further embolism which might well be fatal. At the time of ligation it may be possible to remove the thrombus from the vein by suction. Anticoagulant therapy alone may not be adequate in the face of thrombi already formed if pulmonary embolism occurs or recurs during its use, vein ligation should be done at once. Even this ligation, however may not be a panacea although it is usually effective patients have been observed in whom a dangerous thrombosis above the site of the ligatures has followed the operation. In rare cases it has been found necessary to ligate the inferior vena cava.

Pulmonary embolectomy first carried out nearly two decades ago (1924) has not proved to be feasible, at least as a routine measure. Although it may conceivably be actually lifesaving in rare cases, it is a radical procedure which may readily tip the delicate balance of the scales the wrong way It is not a simple operation in itself It may not reach the offending emboli which may be out of reach in both lungs, and in the majority of cases of pulmonary embolism recovery occurs without it.

Prevention of the leg phlebothrombosis that gives rise to pulmonary embolism is more important than its treatment. In the first place a state of physical and especially circulatory fitness should be established and maintained so far as possible, especially prior to surgical operation. At the time of operation as little as possible should be done, especially in older persons, and positions on the operating table conducive to blocking of the pelvic and leg veins should be avoided so far as possible. Postoperatively and in any prolonged illness, as from heart failure, the leg circulation should be fostered by massage, passive and active exercise, and getting the patient out of bed at the earliest possible moment. The routine postoperative use of the anticoagulants heparin and Dicumarol is open to question cases very prone to phlebothrombosis, however should be so treated.

Differential diagnosis. The four conditions with which pulmonary embolism is most commonly confused are pneumonia, congestive heart failure, acute myocardial infarction, and paroxysmal tachycardia. The differentiation is usually easy by history and physical examination alone, but now and again roentgen ray evidence, or the acute cor pulmonale electrocardiogram, or the course of the illness with recurrent attacks solves the problem. The hardest cases are those in which two or even three of these conditions are superimposed. In such patients careful detective work is necessary. The most important clues pointing toward pulmonary embolism are leg phlebothrombosis, recent operation or injury, very abrupt onset, unusual degree of cyanosis, blood spitting of moment, unusually fast pulse and respiratory rates in the presence of relatively slight fever, and recurrence of attacks.

COMMUNICATIONS BETWEEN THE AORTA AND THE PULMONARY ARTERY

There are four types of congenital communication between the aorta on the one hand and pulmonary artery, right ventricle, or right atrium on the other hand. They are: first, and most common, patency of the ductus arteriosus; second, rare cases of a persistent truncus arteriosus without separation into aorta and pulmonary artery; third, exceptional instances of communication between the aorta and pulmonary artery by arterial septal defect, and, fourth, very rare cases of communication between aorta and right ventricle or right atrium by septal defects (see Chapter 13). In differential diagnosis a possible rupture of the aorta into right ventricle or right atrium in bacterial endocarditis and endarteritis has already been mentioned (see Chapter 15), and rupture of aortic aneurysm into pulmonary artery or heart chamber will be discussed below.

ANEURYSMS

Vascular aneurysms (ἀνεύρυσμα, a widening) are most commonly arterial, infrequently arteriovenous. Cardiac aneurysms, so-called, have been described in Chapter 25.

SACCULAR ARTERIAL ANEURYSMS

Arterial aneurysms are not uncommon structural defects, unimportant when small or involving a peripheral artery but often serious, always a potential source of trouble through rupture, and even subject to infection (bacterial endarteritis). Their incidence varies widely since it depends in large part on the incidence of syphilis and trauma in any community and doubtless also on their early recognition and satisfactory treatment. Although partly because of earlier recognition and more satisfactory treatment of these conditions in the last two decades, it is mostly because of prevention that aneurysms are definitely less common in some places than they were a generation or two ago.

In a series of 600 postmortem examinations at the Massachusetts General Hospital in the years 1896 to 1900 there were six individuals (1 per cent)

who had syphilitic aneurysms, four of the aorta and two of the innominate artery while in three more recent series of 600 autopsies each at the same institution in the years 1926 to 1930, 1936 to 1938 and in 1950 there were three cases (0 5 per cent) two cases (0 3 per cent) and one case (0 16 per cent) respectively with syphilitic aneurysms five of the aorta and one of the innominate artery Mycotic and dissecting arteriosclerotic aneurysms are not included in these figures. Altogether there were 54 aortic and 3 innominate syphilitic aneurysms in the first 5 600 autopsies at the Massachusetts General Hospital in a period of 33 years (just prior to 1930) There were in this same series 10 dissecting aneurysms of the aorta and a few mycotic aneurysms, figures of which it is difficult to be certain about, since they have been carefully looked for only in recent years.

The diagnosis of syphilitic aneurysms was made clinically at the Massachusetts General Hospital in 113 of 51 875 patients (0 2 per cent) during the decade from 1900 to 1910 and in only 61 of 75 184 cases (0 08 per cent) during the decade from 1925 to 1935 despite the improved roentgenologic facilities for diagnosis. These percentages show a marked reduction in recent years and are probably significant of a decreasing incidence of aortic syphilis in New England, as evidenced also by a decreasing incidence of syphilitic aortic regurgitation.

In a series of 12,000 postmortem examinations in Philadelphia 306 intracorporeal arterial aneurysms of all kinds were found in 268 patients (2.1 per cent) (Lucke and Rea, 1921)

Etiology *Cause* Syphilis is the most common cause of arterial aneurysms of the aorta and other great vessels of the trunk, about 90 per cent of such aneurysms being produced by this infection. Arteriosclerosis has relatively recently become recognized as the next most frequent cause of aortic aneurysms, especially in the abdomen though in the thorax arteriosclerotic aneurysms are rare (Ruffin, Castleman, and White, 1941) Trauma is the commonest cause of arterial aneurysms in the extremities, with the infections of bacterial endarteritis and rheumatic fever and congenital weakness of the arterial wall acting as infrequent factors.

Age Because of the great preponderance of syphilis as a cause, large arterial aneurysms are generally found in middle-aged persons, forty to fifty-five years old. However syphilitic aortic aneurysms may be found quite frequently in younger individuals also, especially in Negroes, even before the age of thirty years, and rarely in children with congenital syphilis. Traumatic and nonsyphilitic infectious aneurysms may occur at any age but are most frequent in youth.

Sex There is a great male preponderance in the incidence of aneurysm because of the far greater frequency in the male sex of the two chief causes, syphilis and trauma The ratio of male to female incidence is about 10 to 1

Race Aneurysms are found 6 to 8 times more often in Negroes than in white people not only because of the greater incidence of syphilis in Negroes

but probably also because of its less satisfactory treatment among them and particularly perhaps because of the heavy type of Negro labor

Pathology An arterial aneurysm consists of a marked dilatation of an artery local or general, saccular or diffuse; it ordinarily signifies a local bulging of the wall to form a sac. The larger arteries are more often the site of aneurysms than are the smaller arteries because they are more often the seat of an infection which weakens the wall, especially syphilitic mesaortitis, and because they are under greater strain. Of the larger arteries the aorta is most often involved and the ascending portion of the aorta more frequently than any other part, because it is the usual location of syphilitic aortitis. The relative frequency of aneurysms of various arteries was found to be as follows in two series of 530 cases (Crisp, 1847) and 1 000 cases (Klotz, 1926) respectively

Table 13

LOCATION OF ARTERIAL ANEURYSMS

	Crisp	*Klotz*
Thoracic aorta	175	610*
Popliteal artery	137	
Femoral artery	66	
Abdominal aorta	59	108
Carotid artery	25	
Innominate artery	20	
Subclavian artery	23	
Axillary artery	18	
External iliac artery	9	
Cerebral artery	7	
Common iliac artery	2	
Posterior tibial artery	2	
Gluteal artery	2	
Pulmonary artery		
Brachial artery	1	
Subscapular artery	1	
Ophthalmic artery	1	
Temporal artery	1	
In the brain		153
I egions other than brain nd aorta		207

* In 21 of these cases there were aortic aneurysms in both thorax and abdomen

The relative frequency of sites of aortic aneurysms is about as follows on a basis of 10 for aneurysm of the ascending aorta, ascending aorta 10 aortic arch 7 descending thoracic aorta 3 abdominal aorta 3 The chief sites of aneurysms other than in the aorta are the popliteal femoral, carotid, subclavian, innominate, axillary and iliac arteries, and the chief sites of visceral aneurysms are the splenic and hepatic arteries.

As noted above, the chief cause of peripheral aneurysms in arms and legs, is traumatic with bulging of the wall at the site of stab or gunshot wound, or of crushing injury there having occurred a partial healing of the original lesion. The chief cause of *cerebral aneurysms* is a congenital defect of the

wall of the circle of Willis at a junction of the vascular ring with one of the incoming branches in the course of years, amounting to 30 or 40 or more, the thin wall bulges at this point to form an aneurysm of about the size of a pea; it is the rupture of this aneurysm in certain of the cases that gives rise to the important, not very rare *subarachnoid hemorrhage* which abruptly indicates its presence by headache, blood in the spinal fluid, and sometimes syncope and death, though recovery not infrequently occurs. Although syphilitic mesaortitis (see Chapter 16) is the commonest cause by far of thoracic aortic aneurysm, *arteriosclerosis* is a common cause of *abdominal aortic aneurysms* and may even account for an occasional thoracic aneurysm. An interesting variant is the *senile ectasia of the ascending aorta* due to loss of elasticity and occasionally noted in old men or women without syphilis rarely does it reach the size of large syphilitic aneurysmal dilatation. Ruffin, Castleman, and White (1941) analyzed 9 600 autopsy records of the Massachusetts General Hospital and found 60 syphilitic aneurysms of the thoracic aorta and only 3 syphilitic aneurysms of the abdominal aorta, in contrast to 27 arteriosclerotic aneurysms of the abdominal aorta and only 3 arteriosclerotic aneurysms of the thoracic aorta In this same series there were 3 cases of well-marked senile ectasia of the thoracic aorta. On the other hand, Scott (1944) reported that of 62 cases with aneurysms of the abdominal aorta 74 per cent were syphilitic, 21 per cent arteriosclerotic, and 5 per cent mycotic.

A weakening of the arterial wall, chiefly through the destruction or break of the muscular and elastic tissue, causes a local or general stretching, which in turn results in dilatation (Figure 143 page 748) If the process is gradual, enormous outpocketings may occur so that saccular aortic aneurysms may develop of the size of the heart itself or even of a person s head. Usually death from rupture, heart failure, angina pectoris, or other complication takes place before an aneurysm can become very large, especially if the process is rapid or the wall very weak. The aneurysmal lining may be smooth or wrinkled, atheromatous or ulcerated, and the sac may be so filled with thrombus that it pulsates little or not at all. Organization of the thrombus with little or no progression of the syphilitic process may follow a virtual repair of the aneurysm.

A bacterial infection of the arterial wall, usually a complication of subacute bacterial endocarditis, may result in a so-called *mycotic aneurysm* When a lesion actually destroys the arterial coats it differs from the usual aneurysmal dilatation of an artery and so is then called a *false aneurysm.*

Rupture of an aneurysm may occur anywhere, an aortic aneurysm ruptures usually into the pericardial sac or a pleural cavity but sometimes into the mediastinum esophagus, trachea, great veins, pulmonary artery or atria, and sometimes even externally through the skin.

Dissecting aneurysms will be considered later in this chapter as a special type.

The effect of aneurysms on the heart and other structures. The heart itself is but little or not at all involved by an arterial aneurysm, even by a large aortic

aneurysm, unless aortic valve or coronary artery mouths are affected, but secondary effects on various tissues or organs in the neighborhood of an aneurysm, due to pressure, are common such effects include erosion of sternum, ribs, and vertebrae, obstruction and displacement of pulmonary artery esophagus, and trachea, collapse of a lobe of the lung, and irritation or destruction of contiguous nerves causing pain or paralysis, as in the case of pupillary and laryngeal abnormalities.

Symptoms. There are no symptoms of aneurysms themselves except as they cause pressure on surrounding structures (giving rise to dyspnea, dysphagia, cough, hoarseness, and pain) or affect the heart by their complications (giving rise to congestive failure or angina pectoris) It is of considerable interest to know that even large aneurysms may be symptomless, the slow stretching and erosion of the arterial wall itself not ordinarily causing pain.

Signs. Signs of aneurysms are frequent but not always clear without complete examination the condition may remain undiscovered. Signs are due in the first place to the vessel enlargement itself which may be seen or felt, or if in the deeper part of the thorax, observed by roentgen ray examination. The anterior thoracic wall, front of the neck, popliteal spaces, thighs, and axillae are frequently the sites of the pulsating tumors caused by aneurysms bulging the skin and subcutaneous tissues out beyond their normal level. Such aneurysmal swellings may be found even in the back at the left costal margin or in other unusual locations. If an aneurysm is abdominal, intracranial, or deeply seated in the extremities, it may be impalpable and invisible even to the roentgen ray No reliance can be placed on pulsation, systolic murmurs, and palpable systolic thrills over aneurysms they may or may not be present, dependent on the depth of the aneurysm below the surface of the body the elasticity of the wall, the size of the lumen, and the presence or absence of thrombosis. Aside from evidence of arterial enlargement itself there are frequent signs due to pressure on surrounding structures such as are produced by any tumor mass. Arterial pulsation distal to an aneurysm is often delayed and decreased, due not so much to the presence of the aneurysm as to a greater or lesser degree of occlusion of the arterial mouth, which may lie in the aneurysm. The radial pulses are frequently unequal in cases of aneurysm of the thoracic aorta, and sometimes one pulse or rarely even both pulses may be absent, adequate circulation being maintained in the arms by collateral blood supply Very rarely clubbing of the fingers may result from inadequacy of the circulation in one hand or in both hands due to the effect of an aortic aneurysm. In aneurysms of the thoracic aorta the Wassermann reaction is usually positive it was found to be positive in 50 cases (82 per cent) among 61 Negroes with thoracic aortic aneurysms (Sanford, 1931)

The most reliable evidence of aneurysms of the thoracic aorta is to be obtained by roentgen ray study especially of those involving the arch or descending aorta, a pulsating bulge of the aorta itself is the roentgen ray evidence (Figure 146 page 770) Both the new electrokymography (see Chapter 8) and roentgen ray study of the contours of heart chambers and great vessels out

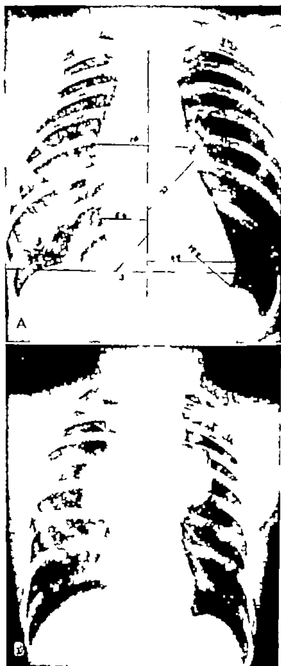


FIG. 146. Roentgenograms showing aortic aneurysms. (*A*) Small aneurysmal bulge of the ascending aorta due to syphilitic aortitis with poorly defined aortic knob and normal heart size. (*B*) Multiple aneurysms of the thoracic aorta with normal heart size.

lined by Diodrast injected into vein or artery can be very helpful in doubtful cases but careful technic and rich experience are usually needed to get the best results. Electrocardiography is of no value in the diagnosis of aneurysms.

On occasion in the absence of roentgen ray examination the very first evidence of an aortic aneurysm has been its rupture, with fatal hematemesis for example.

Course and prognosis. A small traumatic aneurysm may not in any way limit activity or duration of life but a large aneurysm of a large artery especially since it is commonly syphilitic, generally causes death in a few months to a few years and is associated with very serious disease. The usual aortic aneurysm has an unfavorable prognosis, but occasional cases are encountered in which such an aneurysm may remain more or less latent without change for 5 to 15 years with or without special treatment. The most important point, often overlooked, concerning the prognosis and result of treatment of an aneurysm, especially one of the thoracic aorta is that hard physical work has an unfavorable effect on the course of life. The more strenuous the activity the shorter the life and the poorer the result of therapy

Rupture of an aortic aneurysm is not always fatal. Small leaks may heal and even perforation into the pulmonary artery is compatible with months to a year or more of life (Porter 1941 White, Chamberlain, and Kelson, 1941)

Complications. The chief complications of aneurysms, already mentioned, are those due to secondary cardiac involvement, pressure effects on surrounding structures, and rupture.

Treatment. The treatment of aneurysms is of three kinds (1) that of the cause, (2) that of the complications, and (3) that of the aneurysm itself. If syphilis is the cause (as it often is) and there is no heart failure, specific therapy should be instituted with care as outlined in Chapter 16

In earlier editions of this book the reader was warned that the progress of this treatment must be followed in great detail and the heavy metals discontinued if symptoms of cardiac failure appear or if the aneurysm increases rapidly in size apparently as the result of the rapid resolution of the lesion by the drugs, but the introduction of penicillin in the treatment of syphilitic aortitis renders much of this old advice now obsolete.

Serious complications of heart failure and angina pectoris are to be treated as outlined in Chapters 21 and 30 of this book. Pain due to pressure on and erosion of surrounding structures may be relieved temporarily by morphine, but paravertebral alcohol injection or sympathectomy which affords more permanent relief is much to be preferred.

In some cases where an aneurysm is saccular or easily accessible, surgery may be indicated. For a peripheral aneurysm obliteration of the sac has been done by rapid or gradual ligation of the artery in one or several operations, the speed of arterial occlusion, which may be extended over weeks or months, depending on the extent of collateral circulation to the part of the body supplied by the artery involved. A second procedure has been the wiring, with or without electrolysis, of saccular aneurysms of larger arteries like the aorta,

here a coil of platinum, gold, or silver wire is inserted into the aneurysmal sac, preferably under roentgen ray control. The presence of this wire and the passage through it of a small electric current may result in thrombosis in the aneurysmal sac, tending to retard further progress of the lesion and to relieve distress such thrombosis, however is by no means a constant result of this procedure. The third surgical maneuver is to support the affected vessel or sac by surrounding it with strong connective tissue, for example, a sheet of fascia lata, or with cellophane. In August, 1949 Abbott reported having applied cellophane to thoracic aneurysms in 32 instances with internal wiring in addition in four of these patients. The majority of the lesions were syphilitic in origin. On two occasions the procedure was carried out even in the presence of active massive hemoptysis. All of these methods have been employed, but the first is most often applicable and is the method of choice for peripheral aneurysms. Care must be used to ascertain the presence of a sufficient collateral circulation before the artery in question is occluded. The accompanying vein should be ligated with the artery

Differential diagnosis. An arterial aneurysm is usually easy to diagnose, except when it is deep-seated, but when thrombosed it is sometimes very hard to differentiate from a tumor of other nature, especially if that tumor is vascular and pulsating. The close structural relationship to some artery the marked pulsation often present, and the history of trauma, or history or proof of syphilis, are the most important findings favoring a diagnosis of aneurysm. All methods of study must be used in doubtful cases, especially in patients with thoracic and abdominal aneurysms.

DISSECTING ANEURYSMS

Dissecting aneurysms must, like arteriovenous aneurysms, be considered by themselves for they form a distinct though small clinical and structural pathologic group (Shennan, 1934) They involve chiefly the aorta, occasionally the first part of the aortic branches due to extension from the aorta, and rarely other vessels such as the coronary arteries independently

Until the last decade dissecting aortic aneurysms were merely postmortem surprises but now they are frequently recognized clinically as evidenced by the steady accumulation of reports of correct antemortem diagnoses.

Etiology *Cause* The essential cause of dissecting aneurysms is a weakness in the media, in the case of the aorta a medial necrosis of unknown cause (Erdheim, 1929) A second factor usually of great importance, is hypertension. A third factor infrequently is atherosclerotic disease of the arterial wall. Syphilis is only very rarely a contributing cause, apparently in only 2 of 64 cases reported by Mote and Carr in the year 1942. Strain or even trauma may be rarely a precipitating factor (Leonard, 1945)

Age Dissecting aneurysms are found most commonly in middle-aged and elderly subjects, rarely before the age of 30 years. A very young case of dis-

secting aneurysm of the aorta has been reported within the last few years in a boy 15 (McLaurin, 1945)

Sex The male sex is predominantly affected in the ratio of about 3 to 1

Pathology The dissection apparently begins in the media as the result of the rupture of a vas vasorum, but the intima quickly breaks through into the medial lesion by tearing sharply in a horizontal or oblique direction part way around the inner circumference of the aorta in its ascending portion or in the arch, less commonly in its descending portion in thorax or abdomen (Figure 147 page 774) Under a high head of pressure (most of the patients have hypertension) the intra-aortic blood penetrates into the media as a rule splits it extensively up and down, but sometimes only up or down, and occasionally dissects its entire length from aortic valve to bifurcation at the common iliac arteries. The dissection occurs around ½ to ⅔ of the circumference of the aorta, and the blood in the medial split bulges the wall out in a variable but usually only moderate extent of ½ to 1 cm thickness. Secondary tears through the intima are likely to be found at the upper and lower ends of the dissection, even into one of the iliac arteries, thus producing an extra channel through which the blood passes In most cases in the course of minutes, hours, or days the aorta ruptures completely as the result of a tear through the adventitia with sudden death due to extensive hemorrhage into pericardial or pleural cavity in a few cases the lesion heals sufficiently so that the extra aortic channel becomes lined with endothelium to give a double-barreled aorta. A constant and important complication is the involvement in the process of dissection of the mouths of the aortic branches, with compression of these vessels and resulting effects of the sudden blocking of the local circulation as in the case of an iliac, a coronary or an intercostal artery

Careful search of the aortic wall histologically at the site of rupture has revealed in most cases an area of unexplained degeneration or necrosis in the media.

Symptoms. In a few cases the arterial dissection may apparently be either symptomless or so obscure in its symptomatology that it cannot be diagnosed. As a rule, however there are two symptoms that are more or less characteristic and when added together almost pathognomonic. Pain attending the splitting of the aortic wall is usually excruciating and extensive, radiating from midthorax front or back through the chest, down the back, and even into the thighs or up into the neck. The pain in the thorax or back comes suddenly at its maximum and is often prostrating, inducing a state of shock or even death. If the patient survives, the pain usually lasts for hours, sometimes 24 to 48 hours, requiring morphine repeatedly it may recur if there is an extension of the dissection.

The other important symptom or group of symptoms is dependent on the blocking of the circulation to some important part or parts of the body especially legs, viscera, or brain. Pain, numbness, coma, and other symptoms may result. The very multiplicity of symptoms in some cases aids in the diagnosis.

Signs. There are no pathognomonic signs of dissecting aneurysms. In the case of the aorta, a systolic murmur at the base of the heart, transmitted to neck and along the spine, may be heard, and an aortic diastolic murmur has been noted, but these murmurs are far from constant. Chronic hypertension and some cardiac enlargement therefrom are almost invariably present. The

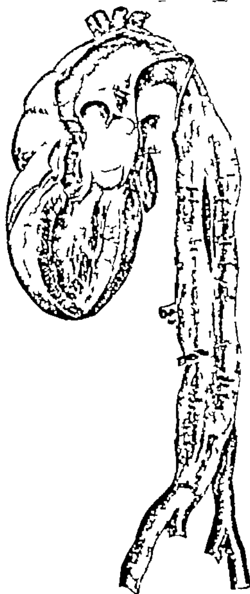


FIG. 147 Drawing showing dissecting aneurysm of the aorta, beginning in the ascending aorta and extending the entire length of the aorta into the common iliacs. (W G MacCallum, *A Text-book of Pathology* 1928 W B. Saunders Company Philadelphia.)

blood pressure often remains high after the dissection occurs or it may sink rapidly and to a low level temporarily during the state of vascular shock that commonly appears, and may rise again with recovery Arterial pulse obliteration may be found, due to compression of one of the aortic branches: this is most commonly observed in the legs where other signs of vascular occlusion develop.

Fever and leukocytosis of slight to moderate degree are common for a few days, or of low grade even for a few weeks, after the dissection of the aortic wall.

Roentgen ray examination is rarely helpful unless a comparison of the shape and size of the aorta in a film taken before the acute illness can be accurately made with the aortic shape and size after the occurrence of the dissecting aneurysm, slight changes in shape and caliber are to be expected. Very rarely a larger bulge than usual of the dissected aortic wall may be noted by roentgen ray with calcified aortic intima visible well within this shadow

Electrocardiography is helpful because of its negative findings except in rare cases where one or the other or both coronary arteries may be involved in the process with more or less occlusion. Usually the electrocardiogram shows no striking change from records taken prior to the acute illness: such records may be expected to show in some cases the hypertensive pattern (see Chapter 19)

Course and prognosis. Dissecting aneurysms of the aorta are usually fatal as the result of rupture through the adventitia in the course of minutes to days in three quarters to four fifths of the cases. Death in such individuals occurs suddenly even though they may seem to be convalescing satisfactorily Certain cases survive a few months to a few years and may die noncardiovascular deaths in some of these the postmortem finding of a double-barreled aorta has been a complete surprise. Sudden death has been reported from spontaneous rupture and dissecting aneurysm of the left anterior descending coronary artery with compression and complete occlusion of the lumen (Helpern, 1947)

Complications. As noted above the chief complications of dissecting aneurysms are external fatal rupture and blocking of the circulation to some part of the body (especially legs, heart, and brain)

Treatment. So far the only treatment for dissecting aneurysms is absolute rest for weeks probably six at least, special nursing care at the onset of the acute illness, and symptomatic therapy by morphine for pain and shock, and for symptoms due to obstruction of various peripheral or visceral arteries. No surgical therapy appears justified as yet.

Differential diagnosis. There are two conditions particularly with which dissecting aneurysm of the aorta is likely to be confused coronary thrombosis and peripheral embolism. The intense thoracic pain followed frequently by a state of vascular shock with drop in blood pressure and later by fever and leukocytosis strongly suggests acute coronary occlusion, but there are certain clues usually present which point to the correct diagnosis the sudden onset of the maximal pain instead of the building up of the pain in the course of a

few minutes as is the case with coronary occlusion pain, the radiation of the pain usually to the back or its original presence there, the radiation of the pain down the back, often to the legs, the evidence of rapid blocking of peripheral arteries before embolism from endocardial infarction is possible, and the usual absence of characteristic coronary changes in the electrocardiogram. Dissecting aortic aneurysm as a cause of blocking of the peripheral arteries can be distinguished from embolism by the initial occurrence of severe chest or back pain just prior to the arterial block (by only a few minutes) and the absence of any adequate explanation for intracardiac thrombosis where the embolus would have to originate.

Pulmonary embolism, another thoracic emergency is less likely to be confused with dissecting aneurysm of the aorta because of the preponderant dyspnea, cyanosis, and tachycardia attending it, with much less pain, a frequent story of recent operation or injury the common occurrence of phlebothrombosis in the legs, and the occasional bloodspitting and localized pulmonary signs.

ARTERIOVENOUS ANEURYSMS

An important vascular lesion, uncommon but of considerable interest, is a direct communication between artery and vein this is called an arteriovenous aneurysm or fistula. It does not include the small vessels which normally may join arterioles directly to venules without the interposition of capillaries that have been found in certain parts of the body as in the fingers (Grant and Bland, 1931) and in the myocardium (Wearn, et al., 1933) Although an arteriovenous aneurysm may occur anywhere in the body and between vessels of any size, it is most common in the extremities between arteries and veins of medium caliber like the popliteal vessels. Usually trauma is the cause, a perforating wound uniting an artery with a vein either directly or by rupture of traumatic aneurysm, hematoma, or infected area. Such a fistula may result accidentally from surgical operation. Much less often primary arterial disease, namely infection, ulceration, or aneurysm is responsible, as in the case of the rupture of an aneurysm of the ascending aorta into the superior vena cava. A congenital arteriovenous aneurysm is not so rare as was once thought it is an infrequent but important anomaly of the pulmonary circulation, resulting in cyanosis and cardiac enlargement.

The short circuit of a considerable amount of blood produced by a large arteriovenous aneurysmal shunt has three chief effects. In the first place, the vein is widely dilated, the dilatation extending generally far along the course of the vein distending the valves if present, and rendering the vein incompetent. There is seen and felt a marked arterial pulse in the vein, and a blocking of venous blood flow occurs distal to the aneurysm. The artery also takes part in the dilatation, but to a much smaller degree. In the second place, a loud often roaring, continuous murmur with systolic accentuation and a palpable continuous thrill, is evident over an arteriovenous aneurysm of large or average size, even when it is deep-seated. These signs are the chief basis for the

diagnosis. In the third place, the lesion may be serious because of the effect on the heart, the left ventricle becoming considerably enlarged except when the arteriovenous aneurysm is small. The blood flow is much increased by an arteriovenous shunt of large size, and it is this fact that is doubtless responsible for the effect on the heart.

An interesting lesion, which, like patency of the ductus arteriosus, has an effect on the heart and circulation similar to that of an arteriovenous aneurysm or shunt is perforation of the aorta into the pulmonary artery—here the blood stream goes from the high pressure systemic circulation into the low pressure pulmonary circulation with deleterious effect, death if the perforation is large, heart failure if small.

The course and prognosis are unfavorable with arteriovenous aneurysms of large size unless they can be treated, heart failure developing in the course of a few months or years. A communication between aorta and superior vena cava is especially serious, death coming as a rule quickly in a few hours, days, or weeks. Rupture of the arteriovenous aneurysm is an occasional complication.

The treatment consists of ligation of the arteriovenous aneurysm, about three months after the development of the lesion, if traumatic (to allow the establishment of an adequate collateral circulation) if such ligation is possible. Rapid relief usually follows ligation with decrease or disappearance of cardiac enlargement and prevention of heart failure. A case of cure of Streptococcus viridans infection of an arteriovenous aneurysm by excision of the aneurysm was reported by Hamman and Rienhoff in 1935

PERIPHERAL VASCULAR DISEASE

Although peripheral vascular disease is often set off by itself as a special province and is per se widely spread throughout the entire body nevertheless it forms but a part of the larger realm of cardiovascular disease and has frequent and intimate associations with diseases of the heart and great vessels.

DISEASES OF ARTERIES

Some of the more intimate associations have already been referred to, such as *periarteritis nodosa* which is in reality a systemic disease involving many parts of the body including the coronary arteries, damage to which can seriously affect the heart (see Chapters 21 and 23) Arterial obstruction by *thrombosis* superimposed on *sclerotic disease* or *endarteritis obliterans* (Buerger's disease) can jeopardize the health and result in gangrene of the legs, especially in men already laboring under the strain of some type of heart disease, usually coronary or hypertensive or both, and *arterial embolism* may be a serious complication and even precipitate death in patients with rheumatic heart disease, subacute bacterial endocarditis, and coronary heart disease (see Chapters 14 15 and 21) On the other hand, *intermittent claudication* which consists of leg muscle ache, especially in the calves, on walking, due to insufficient blood supply secondary to arterial obstruction, may limit the activity of

a patient with coronary insufficiency to such degree that this more important disease is less of a hazard to life. *Endarterectomy* recently introduced in France (Leriche, 1946 Bazy 1948 Laubry and Reboul, 1950) has been an effective new therapeutic measure helping certain cases of arterial obstruction much more than have vasodilating agents and sympathectomy although aminophylline has helped some cases (Kissin et al., 1951)

Arterial spasm is an occasional disturbing accompaniment of venous thrombosis in the extremities or of arterial embolism and as a special entity produces the important condition of *Raynaud's disease* (Raynaud, 1862) which, giving rise at first to the syndrome of dead fingers (doigts morts) can progress to serious structural changes in the tissues and even to gangrene (see Chapter 31) There is still some question as to whether either arterial spasm or endarteritis obliterans of the Buerger type affects the coronary circulation.

Arteriosclerosis of the media of the arteries of the limbs, so often found in laborers and called *Mönckeberg s sclerosis* (Mönckeberg, 1924) is an entirely different process from the atherosclerosis of coronary and cerebral arteries and aorta as a matter of fact I have very infrequently found tortuous, calcified, and beaded radial arteries in my patients with coronary heart disease, whose radials are usually soft, and similarly have infrequently noted coronary heart disease in cases with Mönckeberg s peripheral arterial sclerosis.

Aneurysms saccular due to syphilis, mycotic involvement, arteriosclerosis, and trauma *dissecting* and *arteriovenous* all of which may have an important effect on heart and great vessels, have been discussed in some detail earlier in this chapter

DISEASES OF VEINS

The most common diseases of the *veins* are *thrombosis* and *varicosities*. The former in its most important relationship of leg vein thrombosis has been discussed earlier in this chapter in the section on Pulmonary Embolism; another important, though rare, abnormality is that of thrombosis of the great veins, particularly the venae cavae, an example of which is illustrated in Figure 148 Pressure by surrounding structures (e.g. tumors) trauma, infection, and stasis are causative factors If the superior vena cava is blocked, the so-called superior mediastinal syndrome results, and if the inferior vena cava is thrombosed high up there develops the inferior mediastinal syndrome. Varicose veins are more of a nuisance than a serious disease but, on occasion, they may be associated with ulceration and infection and, when very extensive, may actually give rise to circulatory insufficiency due to the pooling of enough blood in huge varicose veins so that there is a serious reduction of the volume of blood returned to the heart with resulting faintness and dizziness (Chapman and Asmussen, 1942) *Venous spasm* is an interesting phenomenon which may on occasion, cause difficulty as in occasional instances of cardiac catheterization.

Portal and splenic vein thrombosis can be very serious with obstruction and ascites resulting therefrom as also from hepatic cirrhosis which may require consideration of portocaval anastomosis via renal circulation or vena cava

directly One of the important complications of such diseases is dilatation of the esophageal varices that are so prone to bleed freely

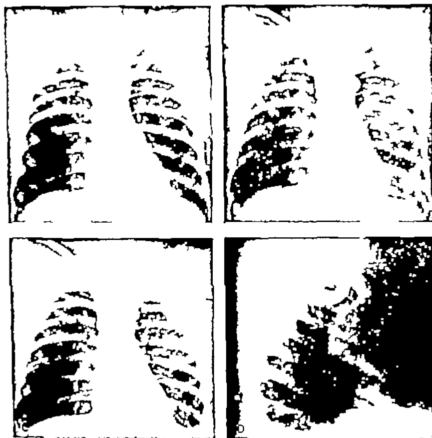


FIG. 148. Roentgenograms of thorax showing visualization of great veins by Diodrast injection. Case of young man with traumatic block of superior vena cava indicated clearly in (*B*) and not visualized in the control record (*A*) (*C*) Film taken shortly after (*B*) showing filling of vena azygos minor and pericardial vein. (*D*) Oblique view shows very well the large collateral vessel, vena azygos minor taking blood from the upper superior vena cava down to the abdomen to empty into the inferior vena cava. (With the kind help of Dr George P Robb, 1 Madison Ave., New York City)

For further discussion and details of the etiology diagnosis, and treatment of peripheral vascular disease the reader is referred to the references to publications in the Bibliography at the end of this chapter

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PART IV

DISORDERS OF CARDIOVASCULAR FUNCTION

CHAPTER 29

THE CIRCULATION OF THE BLOOD
IMPORTANCE OF DISORDERS OF CARDIOVASCULAR FUNCTION
CLASSIFICATION OF TACHYCARDIA, BRADYCARDIA, AND ARRHYTHMIA

Although William Harvey announced his discovery of the circulation of the blood over three hundred and twenty years ago (1628) it has been only within recent times that the circulation as a whole has been properly understood. The heart is but the central organ though it is, to be sure, the most important link in the chain. Even the blood vessels, vital though they be, do not complete the picture. It will be worthwhile for a moment to survey the various detailed parts of the body that share in the fascinating process of getting the blood to go where it should. Let us start with the right atrium, where at its junction with the superior vena cava lies the pacemaker the ultimum moriens, the sinoatrial node with its automatic control of the heartbeat chemically mediated by important autonomic nerves which pass on the signals from the rest of the body as to its circulatory needs with particular respect to rate. The volume and speed of the blood returning to the right atrium from all the body tissues also act reflexly to govern the action of the heart. Besides being the pacemaker the right atrium has great capacity as a storehouse to aid in preventing the overdistention of the rest of the heart; furthermore the tricuspid valve is, as stated by King over a hundred years ago (1837) the safety valve of the heart, helping to keep it from being overloaded. The pulmonary artery and its branches, like the aorta, by their elasticity maintain a fairly even flow of blood through the lungs instead of the forceful systolic jets, both uneconomical and harmful, that would be imposed on the delicate capillary structure of the pulmonary alveoli were they rigid tubes. The wonderful network of tiny vessels ramifying through the lungs not only is an ideal mechanism for exchange of gases and water between blood and alveolar air but possesses such rich anastomoses between all the larger vessels, and with the bronchial cir

culation, that actual blocking of one of the good-sized pulmonary arterial branches is not usually followed by infarction unless there are complications of serious cardiac or pulmonary disease also the pulmonary circulation in its many ramifications can hold much extra blood, if necessary without great difficulty

The act of breathing not only serves for the exchange of gases between atmospheric air and blood, but it has another very important and frequently overlooked function, namely to suction blood from outside the thorax into the great veins by the establishment of a negative pressure on inspiration and to drive blood forward by positive pressure on expiration. This is one of the important reasons for deep breathing or other exercises to keep the diaphragm and accessory respiratory muscles fit.

The great elasticity and strength of the aorta and its main branches are factors of major importance in maintaining an even and economical systemic blood flow a function often overlooked. Next, the arterioles should be noted, an amazing autonomic mechanism for the control of the circulation in any or all parts of the body: dilatation brings more blood to the organ or tissues where it is needed and keeps the blood pressure from mounting dangerously while constriction helps to divert blood from any part of the body where it is not needed to other parts which are active.

The capillaries, first identified by Malpighi in 1661 are the vessels for which all the rest of the structures of the circulation were originally set up. In their loops there is a balancing between the hydrostatic pressure and the osmotic pressure whereby oxygen, needed salts, and nutritive fluids seep through to the tissues, and the waste products, carbon dioxide, and excess fluids pass back into the capillary blood stream. There is a smooth and effective gradient of blood pressure all the way from the heart or aorta itself to the venae cavae.

Next, the veins of the body are endowed with two mechanisms that aid greatly in the maintenance of the circulation (1) the valves which normally prevent the blood from going the wrong way and (2) the proximity of skeletal muscles which by their contractions and maintenance of good tone compress the veins and help to send blood back toward the heart. Thus the important accessory aid to the circulation of blood rendered by diaphragm and skeletal muscles is reason enough to keep the whole body physically fit.

An interesting and essential convenience in the circulation is the portal system actually a third subdivision of the total cardiovascular tract. Here, economically food products are directly taken up and stored or utilized by the liver for the body's needs

The renal circulation carries out one of the most interesting and vital functions of the body acting as a highly selective filter of the blood to rid the body of nitrogenous waste products and excess fluid and to regulate the balance of electrolytes and water Fortunately there is a great reserve for life can continue actively for many years with but one kidney Damage by infectious toxins, other bacterial invasion, and metallic and other poisons

accounts for most of the kidney diseases of early life. To combat the acute renal shut-down in such cases there has been introduced in late years a most ingenious artificial kidney reference to which can be found in the Bibliography attached to this chapter In later life, vascular changes of the renal circulation account for the slowing down of renal function sometimes with acute changes, but usually with a condition called chronic arteriosclerotic nephritis.

Finally the lymphatic system is a very important accessory to the circulation of blood, acting to take care of all the infectious processes and foreign bodies and to perform miscellaneous tasks that cannot be readily accomplished by the cardiovascular system per se.

DISORDERS OF CARDIOVASCULAR FUNCTION

And now last in our consideration of cardiovascular disease, come disorders of circulatory function, and rightly so, for important and superficially impressive though they may often be, they are fundamentally of less importance than the etiologic factors back of the cardiovascular disease and the structural defects that such etiologic factors leave behind them. Disorders of circulatory function fit into two groups serious disturbances, often end results, of severe cardiovascular disease, and trivial or at any rate relatively unimportant conditions with or without such disease. Neither of these two groups should assume the major importance sometimes ascribed to disorders of function. The doctor must of course recognize and properly treat these troubles, but it is far more important for him to analyze and treat so far as possible the etiologic factors behind present or future cardiovascular disease in individual or family and to search for structural defects which may some day cause serious disorders of function, protection against heart disease and cardiovascular failure is far more vital, foresighted, and profitable than the treatment of the failure itself

Although a few disorders of circulatory function are of great importance, the majority are negligible or of but slight importance a careful analysis of functional disorders is essential, therefore, to differentiate the serious from the benign. The most severe disorders which are likewise of great frequency are *congestive heart (myocardial) failure general vascular failure* and *coronary insufficiency causing angina pectoris* associated with myocardial failure are the grave conditions called *cardiac asthma* and *pulsus alternans* The first two of these disorders will be discussed in the next two chapters. The third has already been discussed in Chapter 21 *Disturbances of heart rhythm*, though much emphasized during the time of the development of their special study and analysis, are of far less general importance than are myocardial failure and coronary insufficiency· nevertheless, it is necessary to recognize and to understand cardiac arrhythmia thoroughly in order to give a wise prognosis and to prescribe good treatment. Disturbances of heart rhythm include premature beats (atrial and ventricular) paroxysmal tachycardia (atrial and

ventricular) atrial fibrillation, atrial flutter depression of the sinoatrial pacemaker atrioventricular nodal rhythm, ventricular escape (also called interference dissociation and reciprocal rhythm) atrioventricular block, and intraventricular (bundle branch) block. These disorders will be discussed in the three final chapters of the book. Among them the only grave conditions are paroxysmal tachycardia of ventricular origin and high-grade heart block, both of which are rare. Intelligent treatment of these and of the other disorders of heart rhythm, most of which are very common, affords the affected patient much relief of mind as well as of body

Circulatory failure may be subdivided in a somewhat different way from that just mentioned into the following (a) heart muscle failure secondary to specific strains such as valvular disease, hypertension, and myocardial destruction which involves either left ventricle, right ventricle, or the whole heart; (b) obstruction to the circulation with resulting congestion behind the obstruction, for example, congestion of the lungs from the mechanical effect of mitral stenosis and congestion of the liver from the mechanical effect of tricuspid stenosis or of acute or chronic constrictive pericarditis (c) failure of the coronary blood supply to the heart muscle (d) serious failure of cardiac rhythm due to ventricular fibrillation or cardiac standstill. An interesting further subdivision of myocardial failure is into that in which there is the usual myocardial insufficiency with a decreased blood flow as in the case of hypertension or valvular disease and that in which there is increased blood flow as in the case of thyrotoxicosis, beriberi, arteriovenous fistula, and anemia.

The disturbances of normal physiology responsible for these various disorders of cardiovascular function will be taken up in each chapter under the first heading "mechanism," but for more detailed discussion of symptoms and signs blood pressure blood flow blood gases, and graphic records the reader is referred to Part I of this book.

An important part of the functional diagnosis in a cardiac patient is some sort of statement of *actual physical capacity* at the time of examination. This is best expressed not by any set standards or functional tests but by the ability of the patient to carry on his routine daily activity a variable which must be considered individually for every patient. A simple classification of this functional capacity is as follows

1 Full normal activity possible without cardiac symptoms.
2. (a) Activity slightly restricted by symptoms.
   (b) Activity moderately restricted by symptoms.
   (c) Activity greatly restricted by symptoms.
3 No activity possible without symptoms.
4 Symptoms even at rest.

Thus a complete cardiovascular diagnosis should include four features first etiology second, structural change third, disorders of function, and, fourth, physical capacity The following are examples of complete diagnoses

Rheumatic heart disease with mitral stenosis, atrial fibrillation, and congestive failure· activity greatly restricted by symptoms.

Congenital cardiovascular disease with patency of the ductus arteriosus full normal activity possible without symptoms.

Syphilitic aortitis with aortic regurgitation and angina pectoris, symptoms even at rest.

Hypertensive heart disease with activity slightly restricted by dyspnea.

Although a large part of the treatment of functional circulatory disorders must be symptomatic, it is equally important, as I have suggested a few paragraphs earlier to treat the underlying diseases when possible and especially to try to practise preventive medicine. Fortunately more attention is being paid at the present time than formerly to the prevention of disease, and, when disease is already present, to the prevention, so far as is possible, of the further progress of that disease and of the failure of function. Such measures are especially applicable to diseases of the heart. Not only must we try to abolish conditions which cause structural abnormalities of the heart, but we must attempt in the presence of such abnormalities to keep strain from inducing functional disorders. Here the occupational training and placement of cardiac patients is of great importance Sound judgment of all the factors involved—training, mental ability physical capacity family responsibility opportunities, happiness, and preferences of every individual patient—must decide the matter of work for each case, rather than any set of rules or standards, no matter how elastic. Many measures, such as attendance at health resort, sanitarium, and spa, are far more fruitful when used in a prophylactic way than when used in therapy Sound advice which is heeded is worth an immeasurable amount of medicine, and the wise and careful regulation of living almost always adds to the duration of life, to its fullness, and to its accomplishments, whether slight or serious heart disease be present.

In this introductory chapter it will be of value to consider the disorders of the heartbeat from the standpoint of general classification according to rate and rhythm, to supplement their individual consideration in later chapters. The following tabulation gives the various types and causes of tachycardia, bradycardia, and arrhythmia. The terminology employed throughout the book has been changed in accordance with the new international nomenclature to "atrial" and "atrio-" instead of "auricular" and "auriculo-"

TACHYCARDIA

Tachycardia (ταχύς, quick, and καρδία, heart)

1 **Sinoatrial tachycardia.** This consists of regular rapid heart action, as a rule at rates in the adult between 80 and 160 per minute, with gradual onset and offset, and is generally due to the combined effect on the sinoatrial node of depression of vagal action and of stimulation of sympathetic nerve action, and less often to either effect alone. Rarely the rate may rise above 160, even

to 200 or more. The normal heart rate of the young infant varies from 100 to 150 at rest and of the child below adolescence from 80 to 120 though there are frequent exceptions with slower rates.

The causes of tachycardia are

a. Normal mechanism in some healthy individuals (but not over the rate of 100 in adults at complete rest)

b. Physiologic reaction to exertion, ingestion of food, excitement, and pain.

c. Voluntary acceleration. Rare. Due primarily to unusual sympathetic nerve control and attended by increase of blood pressure and by pupillary dilatation. The heart rate may be doubled, as from 80 to 160 The accleration is rapid, requiring a few beats to full speed, and not instantaneous. It is still possible even after paralysis of the vagi by atropine (Favill and White, 1917)

d. Neurocirculatory asthenia, some cases, in part probably due to effort of heart to compensate for a relatively small venous blood return to the heart and in part due to apprehension.

e. Reaction to other factors that reduce considerably the amount of blood returned to the heart, these factors include vasomotor shock, hemorrhage, long standing in the erect position without movement, pooling of blood in extensive varicose veins, and acute and chronic constrictive pericarditis.

f Reaction to certain substances, such as coffee, tea, and tobacco, and to certain drugs, such as epinephrine (adrenaline) via sympathetic nerve stimulation

g. Reaction to drugs, such as atropine, causing decrease in vagal action, and to diseases like diphtheria and poliomyelitis which may cause vagal paralysis.

h. Thyrotoxicosis.

i. Reaction to toxins of infections. With every degree of fever there is an acceleration of approximately ten heartbeats per minute.

j. Reaction to pulmonary embolism.

k. Reaction to heart disease and failure itself.

2. **Paroxysmal tachycardia.** This consists of a regular rhythm at heart rates usually of 120 to 320 per minute, averaging 160, with sudden onset and offset. The fastest rates are found in young infants. The duration of paroxysms varies from a few seconds to several days, but is usually a few minutes to a few hours.

The causes of paroxysmal tachycardia are, primarily abnormal irritability of the heart and, secondarily various exciting factors heart disease itself is not the usual cause. Complete discussion of this disturbance of cardiac rhythm will be found in Chapter 32. The types of paroxysmal tachycardia are

a. Atrial. Usually ectopic, rarely at, or very near the sinoatrial node. As a rule unimportant but annoying.

b Ventricular Rare. Usually serious.

c. Atrioventricular nodal. Very rare Not serious.

3 **Atrial flutter** This consists of a regular or regularly irregular rhythm, at atrial rates usually of 200 to 400 averaging 300, and ventricular rates

usually at one half the atrial rates, due to 2 to 1 heart block. The onset is sudden. The duration of atrial flutter varies from a few hours to several years, but is usually a few days or weeks. The causes of atrial flutter are, as in the case of paroxysmal tachycardia, abnormal irritability of the heart and various exciting factors heart disease is usually present. Atrial flutter will be discussed fully in Chapter 33

4 **Atrial fibrillation.** This consists of absolute arrhythmia at atrial rates of 300 to 500 per minute, averaging 400 and ventricular rates at about 150 before treatment. Its onset is sudden. It is usually permanent, but in about one fourth of the cases paroxysmal, the paroxysms lasting several hours each. Heart disease is usually present in this disturbance of rhythm but sometimes the condition is wholly functional. Full discussion will be found in Chapter 33

BRADYCARDIA

Bradycardia (βραδυς, slow and καρδια, heart)

1 **Sinoatrial.** This is due chiefly to preponderance of vagal action on the sinoatrial node. The rhythm is regular or irregular (sinus arrhythmia) at heart rates of 30 to 60 usually about 45 The causes are

a. Normal mechanism in some individuals, even at a heart rate in the 30s in a few distance runners at rest.

b. Physiologic reaction to rest, sleep vagal stimulation by carotid sinus pressure in the neck or by ocular pressure, and sometimes to cold and fright.

c. An occasional reaction to convalescence from certain infectious diseases, for example, influenza, especially in youth, and often after childbirth.

d. Reaction to increased intracranial pressure (hemorrhage, tumors, meningitis)

e. Reaction to certain diseases hepatitis with jaundice, mumps.

f. Reaction to drugs, especially digitalis.

2. **Atrioventricular nodal rhythm,** a very rare mechanism, consists of a regular heart beat at about 40 per minute, the atrioventricular node controlling both atria and ventricles. It is a relatively unimportant functional disorder of unknown cause, to be discussed in Chapter 34

3 **Atrioventricular block.** This consists of a regular or irregular rhythm, usually regular (due to 2 to 1 or to complete block) less often irregular (due to frequent dropped beats or to varying grades of block, especially 3 to 2) The atrial rate is usually normal, and the ventricular rate 20 to 60, being about 40 to 50 with partial block, and 30 to 40 with complete block. It is usually of organic origin. Full discussion will be found in Chapter 34

ARRHYTHMIA

Arrhythmia (privative, not, and ρυθμος, measured motion)

1 **Sinus arrhythmia** presents a heart rate usually varying with phases of respiration but sometimes very irregular It is a functional condition only the

heart may be diseased but usually it is not. Further discussion will be found in Chapter 34.

2. **Premature beats (extrasystoles)** may be few or many in number producing a regular irregularity as a rule; they are more frequently found with slow than with fast pulse rates and without than with heart disease. They are caused by excessive irritability of the heart, by exciting extracardiac factors, or by both. Full discussion will be found in Chapter 32. There are several types of premature beats as follows:

a. Atrial. Not followed by compensatory pause. Occasional.

b. Ventricular. Usually followed by compensatory pause. Common.

c. Atrioventricular. There is no compensatory pause if the premature beat controls both atria and ventricles, but there is a compensatory pause if the premature beat is only an escape of the ventricle. Rare.

3. **Atrial flutter.** There is cardiac arrhythmia in only about half the cases of atrial flutter and when the arrhythmia occurs it is usually a regular irregularity.

4. **Atrial fibrillation.** Absolute arrhythmia.

5. **Atrioventricular block.** The ventricular rhythm is often irregular in partial block, but rarely irregular in complete block.

(See above, under Tachycardia and Bradycardia, for other observations concerning these disorders of rhythm.)

RELATIVE FREQUENCY OF DISORDERS OF HEART RHYTHM

To illustrate the relative frequency of the various disorders of the heartbeat shown *electrocardiographically* among individuals who consult medical advice because of cardiovascular symptoms or signs, I am adding herewith the findings in the order of frequency among 10 000 patients electrocardiographed at the Massachusetts General Hospital in the sixteen years from 1914 to 1931: atrial fibrillation 1 422 cases (14 22 per cent), ventricular premature beats 974, partial atrioventricular block (including 296 cases with long *P-R* intervals without dropped beats) 562, intraventricular block of lesser degree 511, atrial premature beats 512, bundle branch block 223, atrial flutter 104, atrial paroxysmal tachycardia 80, complete atrioventricular block 79, sinoatrial block (including 18 cases of atrial standstill) 61, atrioventricular nodal premature beats 17, ventricular paroxysmal tachycardia 14, atrioventricular nodal rhythm 14, and atrioventricular nodal paroxysmal tachycardia 4 (0.04 per cent) (White and Sprague, 1931).

A more recent review of the index files of the electrocardiograms of the Massachusetts General Hospital covering the nine years from February 1934 to January 1943, including 25 000 patients, has shown a different incidence of disorders of cardiac rhythm, doubtless due in part to the more routine use of this method of study. Hence the new figures are a somewhat better indication of the true incidence of these disorders. Ventricular premature beats led the list, being found in 2,007 cases; atrial fibrillation was second with 1 620 cases, partial a v block third with 1 135 cases; full bundle branch block

fourth with 1 040 cases, atrial premature beats fifth with 984 cases, and then in order intraventricular block of lesser grades (363 cases) atrial paroxysmal tachycardia (151 cases) atrial flutter (139 cases) complete a-v block (104 cases) s-a block (65 cases) a-v nodal premature beats (43 cases) ventricular paroxysmal tachycardia (36 cases) a-v nodal rhythm (32 cases) and a-v nodal paroxysmal tachycardia (15 cases) (analyzed with the kind help of Louise Wheeler)

The relative frequency of the various disorders of the heartbeat actually experienced by patients is not fairly represented by the data obtained from the analysis of electrocardiograms since transient arrhythmias, chiefly in the form of premature beats or extrasystoles, are frequently missed in the short records usually taken. It is quite certain from clinical analysis that ventricular premature beats are several times, probably many times, more common than atrial fibrillation, which happened in the first series of cases noted above to be the commonest disorder found electrocardiographically· also, for the same reason, paroxysmal atrial tachycardia is undoubtedly much more common than the figures given here suggest.

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CHAPTER 30

MYOCARDIAL INSUFFICIENCY (CONGESTIVE HEART FAILURE)
DIGITALIS THERAPY DIURETIC DRUGS

Even though heart muscle failure is usually a late and often the final event in the course of heart disease and so of less fundamental importance than the earlier stages and especially in comparison with preventive measures, it is nevertheless a very serious condition demanding early recognition and adequate treatment. Fortunately although there still remain obscurities about its pathogenesis, there have been important advances both in the understanding of its mechanism and especially in its treatment since the last edition of this book.

Myocardial insufficiency giving rise to congestive heart failure is the commonest of the important functional disorders of the heart. It develops eventually and often terminally in more than half of all individuals with organic heart disease it also occurs in a few individuals without organic heart disease but with sudden abnormal strain, as in the case of massive pulmonary embolism or of prolonged and extreme paroxysmal tachycardia in infancy

An unsatisfactory designation for severe congestive heart failure once customary in France but now being discarded was "asystolie this means literally cardiac standstill which would quickly precipitate death.

Mechanism (abnormal physiology). Under the effect of strain of various kinds the heart muscle may be unable to maintain a satisfactory circulation, so that vascular stasis in various parts of the body results. Such stasis, when it produces symptoms or signs, is called congestive failure, but the myocardium often weakens long before gross signs of congestion appear and various body structures and tissues, such as the kidneys and the brain, may suffer from a resulting lack of adequate circulation. Myocardial failure may come suddenly or slowly The strain is for the most part unilateral at first and one ventricle begins to fail before the other or when both ventricles fail together the weakness of one may be preponderant. Moreover failure of the left ventricle soon adversely affects the right ventricle.

Failure of the myocardium has a twofold deleterious effect consisting of inadequate blood supply distal to the ventricle involved ("forward failure)

and of congestion or stasis proximal to it or behind it. For many years there has been much controversy as to these effects but now it is generally agreed that both points of view should be accepted and that myocardial failure acts in both ways.

Failure of the left ventricle is the commonest type of heart failure. It may be acute as from massive myocardial infarction or sudden tachycardia superimposed on chronic left ventricular strain, or it may be gradual in its development, from hypertension or aortic valve disease. When left ventricular failure results from the constant severe strain of chronic hypertension, dilatation occurs in the already hypertrophied left ventricle, which is no longer able to pump on all the blood it receives from the right ventricle; the mitral valve may or may not become relatively insufficient; the left atrium is overfilled, the lung vessels are engorged, the pulmonary arterial pressure becomes greatly increased, and the right ventricle, unaccustomed to work against such high pressure which in some cases equals or even exceeds that in the systemic circulation, must increase its activity to make up for the added burden thrown upon it. In such a case, if the sequence of events is slow in development, the right ventricle in its turn becomes hypertrophied and eventually dilates and fails along with the left ventricle. Death may come, however, before the strain on the right ventricle has progressed so far, or even before any right ventricular hypertrophy has had time to develop. The significant effect on the lungs of left ventricular failure was pointed out over a hundred years ago, particularly by Hope (1832).

Hope, J. *A Treatise on the Diseases of the Heart and Great Vessels.* William Kidd, London, 1832.

Page 196. As an obstacle to the circulation operates on the heart in a retrograde direction, the cavity immediately behind it is the first to suffer from its influence. Accordingly all the impediments seated in the aorta, its mouth, or the arterial system, act primarily on the left ventricle, which being likewise exposed to the heaviest burden when the circulation is accelerated, has to conflict against a greater variety of exciting causes of hypertrophy than any other cavity of the heart. On this account, therefore, as well as from the thickness of its parieties, it is subject to hypertrophy in a greater degree than any other.

"So long as the left ventricle is capable of propelling its contents, the corresponding auricle, being protected by its valve, remains secure. Hence, in a great majority of cases, the auricle is perfectly exempt from disease, while the ventricle is even enormously thickened and dilated. But when the distending pressure of the blood preponderates over the power of the ventricle, its contents, from not being duly expelled, constitute an obstacle to the transmission of the auricular blood. Hence, the auricle becomes over distended, and the obstruction may be propagated backwards through the lungs to the right side of the heart, and there occasion the same series of phenomena.

Page 205. "The primary effect of universal obstruction of the lungs by engorgement, is, to produce oedema of their cellular tissue and dyspnoea, whether the latter depends solely on the engorgement or partly also on spasm of the bronchi excited by the irritation of that congestion, is difficult positively to determine.

though the latter is highly probable. To this subject I shall revert hereafter The secondary effect is, to gorge the right side of the heart, and thus impede the return of the venous blood from the system at large which co-operates with the increased energy of the arterial circulation in producing anasarca."

Failure of the right ventricle may be more responsible in some cases for symptoms, signs, and even for death itself than the left ventricular failure that usually comes first. If the right ventricle fails because of the strain of left ventricular failure or of chronic mitral stenosis or extensive pulmonary fibrosis, it is not able to pass on all the blood it receives through the lungs to the left side of the heart, it becomes dilated, the tricuspid valve may be insufficient, the right atrium is engorged, and the blood flow in the coronary sinus, the great and small veins, and capillaries is hampered and often greatly slowed. Dropsy or anasarca, with dependent edema, ascites, and hydrothorax, is the end stage of right ventricular failure. Engorgement of the neck veins was well described as a special sign of dilatation of the right ventricle over 200 years ago by Lancisi (1728)

Lancisi, J M. *De Motu Cordis et Aneurysmatibus* J M Salvioni, Rome, 1728, page 141 (Translation by myself.)

"Dilatation of the right auricle and ventricle leads to two consequences worthy of the greatest consideration and these in turn lead to periodic dilatation of the jugular veins. The first consequence is extreme dilatation of the venae cavae, in which the blood may remain for a long time in copious amount. Secondly the orifice of the root of the vena cava is so enlarged that the [tricuspid] valve cusps no longer close. Hence, it happens that with contraction of the heart blood is expelled from the right ventricle, not only into the lungs through the pulmonary artery but also into the wide open superior vena cava by way of the right auricle, and thence into the jugulars.

Occasionally the heart fails in toto when both ventricles are affected by some common strain such as severe rheumatic carditis or severe anemia. Then both ventricles dilate with resulting congestion in both the pulmonary circulation and the systemic veins the atrioventricular valves may become insufficient.

Certainly the most obvious evidence of advancing weakness of either ventricle is congestion behind that ventricle, in the lungs in the case of the left ventricle and in the great veins and liver in the case of the right. A decrease in the power of the circulation in front of the weakened ventricle undoubtedly commonly occurs too but is much less evident clinically except under certain circumstances, as in the case of the cerebral and coronary circulation in the presence of marked aortic stenosis and failure of the left ventricle, and in the case of inadequate renal function on occasion when the blood pressure falls as the result of weakening of a hypertensive left ventricle even before congestion develops. The most striking instance of "forward failure" of the circulation as a whole is that occurring in vascular collapse with resulting inadequate amount of blood reaching and leaving the heart, rare cases of

extremely rapid heart rates in paroxysmal tachycardia and flutter also belong there (see Chapter 32)

Failure of the left ventricle occurs as a primary manifestation of myocardial insufficiency at least three times more often than does failure of the right ventricle. That this should be so is evident when we compare the relative frequency of the factors (hyperpiesia, aortic valve disease, and myocardial infarction) responsible for left ventricular strain with those (mitral stenosis and pulmonary fibrosis) responsible for primary right ventricular strain (White, 1933 and 1942 Boyer Leach, and White, 1940) that it actually is so is indicated by the far greater incidence of dyspnea in early heart failure than of engorgement of neck veins and liver

The precise way in which the heart muscle under strain dilates and fails is not wholly clear but the fundamental factor is doubtless a chemical one. An excessive content of lactic acid in muscle results from excessive work and is associated with fatigue. Redfield and Medearis (1926) have shown that "the ability of the ventricular muscle of the turtle to develop tension is closely correlated with its content of lactic acid" the more the lactic acid, the less the tension possible.

In the discussion in Chapter 25 on cardiac hypertrophy and dilatation it has already been pointed out that hypertrophy is probably a reaction to abnormal stretching or dilatation of the muscle fibers, but from the clinical point of view except in the occasional cases of acute dilatation of the heart, hypertrophy of either ventricle or of both often progresses very slowly and precedes evident dilatation and failure by a considerable length of time, even by many years such hypertrophy at its onset may not be evident on examination.

The three important changes that have come in the point of view concerning cardiac dilatation and failure in the last generation of medical literature in the English language go back to some of the viewpoints of long ago swept aside by too hasty an interpretation of various findings in our own time. These three changes are as follows (1) the heart is not functionally or even anatomically one organ when it is concerned with strains on any individual chamber since a single ventricle may enlarge greatly without immediate effect on the rest of the heart even though the muscle bands are continuous throughout the heart, and since that ventricle may itself alone fail under strain (2) heart failure shows itself most prominently by the presence of congestion behind the weakened chamber and not so clearly ahead of it (that is, distally) *although there is considerable truth in the points of view of both those who* have supported the "back pressure" theory and those who hold the "forward failure theus—neither one alone tells the whole story· and (3) there is such a thing as acute dilatation of either ventricle or of both although chronic gradual failure is more the rule.

Atrial failure and dilatation are of far less importance than are ventricular failure and dilatation, but they have sometimes a certain amount of significance, as discussed in the chapters on cardiac enlargement and atrial fibrillation.

Etiology *Cause.* Almost any kind of heart strain can eventually cause congestive heart failure, but certain factors are much more important or common than others, and very often several factors are combined to precipitate failure in the same case. The commonest causes of congestive heart failure are valvular defects (mitral and aortic) chronic hypertension, and myocardial infarction from coronary thrombosis. Less common but still very important are severe rheumatic carditis, thyrotoxicosis, extensive pulmonary fibrosis, congenital defects, anemia, and abnormally fast heart rates as in long-continued and uncontrolled atrial flutter atrial fibrillation, and paroxysmal tachycardia. Rare causes are arteriovenous aneurysm, cardiac trauma, thoracic deformities, external pericardial adhesions, and tumors. Left ventricular failure is, as stated above, much more commonly initial than is right ventricular failure because the left ventricle is more often subject to strain, particularly as the result of hypertension narrowing or occlusion of the descending branch of the left coronary artery and aortic stenosis or regurgitation. Special strains affecting directly the right ventricle are also of great importance left ventricular failure (by far the most common of all) mitral stenosis, chronic pulmonary disease including emphysema, and congenital pulmonary stenosis. It has been suggested that bulging of an hypertrophied and dilated left ventricle via the septum into the right ventricle may be an important factor in obstructing the flow of blood through the right ventricle and so favoring the occurrence of systemic venous congestion (the so-called Bernheim's syndrome, 1910) It is doubtful, however how important this is since the increased pulmonary pressure due to left ventricular failure unquestionably plays a much larger role, since the right ventricle can quite readily adapt itself to changes in shape and size of the left, and since pulmonary complications, including embolism, commonly occur in left ventricular strain and weakness and may be easily overlooked (Kinsey and White, 1940)

Certain conditions act on both ventricles more or less equally such as rheumatic carditis, anemia, the abnormal tachycardias (atrial fibrillation, atrial flutter and paroxysmal tachycardia) thyrotoxicosis, generalized coronary narrowing, mitral regurgitation, and certain congenital defects like patency of the ductus arteriosus. Special atrial strain comes with stenosis and regurgitation of mitral and tricuspid valves, with ventricular dilatation, and with certain congenital defects especially interatrial septal defects.

In a person with heart disease failure is often precipitated by a relatively trivial circumstance, such as a slight respiratory infection, overeating, excitement, or slight overexertion, but usually heart failure is of gradual onset without any particular precipitating factor In children acute rheumatic infection is the most frequent immediate cause.

It is of considerable interest and value to differentiate the underlying and exciting causes of congestive heart failure An analysis of 1 000 cases (Boyer Leach, and White 1940) has shown the following fundamental and precipitating factors. The former were hypertension 46 9 per cent (21.3 without and 25 6 with coronary heart disease) coronary disease 41 4 per cent (15 8 with-

out and 25 6 with hypertension) rheumatic heart disease 25 7 per cent, syphilitic 3 0 per cent, cor pulmonale 2.5 per cent, calcareous aortic stenosis 1 0 per cent, congenital defects 0 7 per cent, and miscellaneous and unknown 2.57 per cent. The precipitating factors were atrial fibrillation 14 0 per cent, coronary thrombosis 12.8 per cent, respiratory infection 10 5 per cent, rheumatic fever 6.6 per cent, pulmonary embolism 3.3 per cent, other infections 1 9 per cent, malignant hypertension 1 7 per cent, exertion 1 4 per cent, anemia 1 0 per cent, thyrotoxicosis 0 7 per cent, surgical operations 0.5 per cent, paroxysmal tachycardia 0.4 per cent, indigestion or gallbladder colic 0.3 per cent, cough 0.2 per cent, pregnancy 0.2 per cent, asthmatic attack 0.2 per cent, trauma 0.2 per cent, excessive fluid intake 0 1 per cent, emotion 0.1 per cent, and unknown 43 9 per cent (acting suddenly in 4 8 per cent and gradually in the rest) Thus hypertension, coronary heart disease, and rheumatic heart disease are in the order named by far the most common fundamental causes of heart strain and failure in New England today The most common recognizable precipitating factors are, first, the tachycardia of atrial fibrillation, second, infarction of heart or lungs, and, third, various infections, in particular respiratory and rheumatic however a large percentage of cases fail gradually without evident precipitating factor and these have the poorest prognosis.

Sex. Both sexes are equally subject to congestive heart failure, but it occurs earlier and more severely as a rule in males. Cyclical premenstrual congestion may be the first evidence of heart failure in the female.

Age Congestive heart failure is found more often in old than in young persons, three fourths of all the cases being more than fifty years old. Nevertheless it is seen at all ages, even in childhood, when it is sometimes precipitated by a severe rheumatic pancarditis, which, interestingly enough, affects the entire heart or at any rate the right ventricle so severely that the signs of the congestive failure are almost wholly limited to the systemic and portal circulations (increased venous pressure generalized edema, engorged liver) while the lungs remain free (Walsh and Sprague, 1941)

Pathology There are no lesions characteristic of congestive heart failure. It is a functional condition which is almost invariably associated with organic heart disease. A perfectly normal heart may however fail if it is under sufficient strain in such cases it is a question purely of muscle fatigue with the abnormal chemical state that exists in an exhausted muscle. Much has been written about abnormality and limited reserve of the myocardium as the primary causes of heart failure, while such factors as valvular disease have been considered more or less incidental this point of view is only partially correct. In fact, the older views that certain organic lesions were of prime importance were more nearly right than the recent teaching that the heart muscle is everything and that little else matters. It is of great importance to realize that a heart muscle, strong and even massive and healthy may fail simply from severe strain in its effort to overcome some defect, without sign of any degeneration or inflammation, as is frequently illustrated by the hypertrophied healthy

ventricular muscle in a heart that has failed from essential hypertension (hyperpiesia) and by the hypertrophied healthy right ventricular muscle in a heart that has failed from marked mitral stenosis It is this truth that has not been sufficiently emphasized in the recent past. But it is also true that the heart may fail without structural defects or hypertension when there is some direct deleterious effect on the myocardium as in a severe rheumatic infection or in severe anemia. Such direct myocardial effects are frequently superimposed on chronic structural lesions.

The commonest structural abnormality found with congestive heart failure is cardiac enlargement, consisting usually of both hypertrophy and dilatation, and rarely of dilatation alone dilatation without hypertrophy is found when the failure has been acute and rapid, as with coronary thrombosis or fulminating rheumatic carditis or prolonged extreme paroxysmal tachycardia. Either ventricle may be primarily affected in the long-continued chronic cases both ventricles are involved, it is of more than passing interest that by far the most common cause of enlargement of the right ventricle (beginning as hypertrophy) is chronic failure of the left ventricle and not mitral stenosis or severe chronic pulmonary disease or other factor (Thompson and White, 1936) Frequently the atria are also enlarged in heart failure The myocardium shows an increased content of water in anasarca from congestive heart failure (Gross, 1940) Valvular disease, especially aortic regurgitation or mitral stenosis, is occasionally present. Coronary arterial narrowing is sometimes found, particularly in well-marked cases when occlusion of the descending branch of the left coronary artery causes dilatation and failure of the left ventricle. An adherent pericardium and congenital defects are much less commonly seen, but they do occur in some cases. Generalized arteriosclerosis and aortic atheroma often accompany congestive heart failure, but they are apparently merely incidental. Sclerosis of the superior vena cava has been noted as a sequel of long-continued elevation of venous pressure in chronic congestive heart failure (Gross and Handler 1939)

Summarizing the result of a postmortem study of 102 cases of myocardial failure Clawson in 1924 wrote "Coronary sclerosis of serious degree was present in 22.5 per cent. Myocardial fibrosis was found in a marked or moderate degree in 20 5 per cent and in a slight degree in 30 per cent. There is usually a close correspondence between the situation and the extent of myocardial fibrosis and the distribution and degree of the coronary sclerosis. Myocardial fibrosis is usually due to coronary disease, but occasionally rheumatic infections may give rise to a slight degree of fibrosis. Myocardial strain (hypertensive or nonhypertensive) is not a cause of myocardial fibrosis. Syphilitic myocarditis is rare. Myocardial failure is rarely due to anatomical changes in the myocardium. It may be explained as an exhaustion of the cardiac muscle. True chronic inflammation of the myocardium is very rare. What is commonly called chronic myocarditis is usually myocardial fatigue resulting from the various conditions mentioned above. Approximately half of the cases of myocardial failure show no anatomical changes in the heart muscle The anatom-

ical changes in the heart muscle are seldom sufficient in themselves to cause death. With these statements I agree.

The pathologic effect of congestive heart failure on other organs and tissues of the body is by the production of edema, mostly interstitial in its site (even in the lungs) If very long-continued, edema may result in actual tissue change, especially in the liver but Sherlock (1951) has shown by biopsy that the liver may regenerate after damage (centrilobular hepatic necrosis) resulting from severe congestion, when there is improvement in the circulation.

Symptoms. Since left ventricular strain is far more common than right or biventricular strain, the earliest and chief symptom of congestive heart failure is usually *dyspnea* at rest or on effort not previously causing breathlessness. Such dyspnea is due primarily to any one or more of several factors, most commonly a reflex stimulating the respiratory center and arising in the lungs from congestion of the pulmonary circulation, also the effect of oxygen lack (anoxemia) on the respiratory center and a central reflex arising from acute or subacute distention of the atria and great veins. Cardiac dyspnea from the first mentioned and most common factor namely the pulmonary reflex, which results from failure of the left ventricle and not of the right, must be differentiated from other causes of dyspnea giving rise to such a reflex, namely pulmonary pleural, and bronchial diseases and one other of cardiac origin not associated with heart failure. This other cardiac cause of dyspnea due to a pulmonary reflex is mitral stenosis, which acts mechanically and not by myocardial failure; the mitral ostium is too small to transmit to the left ventricle all the blood that comes to it from the strong right ventricle, especially when there is a tachycardia from effort or excitement or of paroxysmal nature the lungs fill up as a result, as was so well stated by Vieussens more than 200 years ago (1715)—see Chapter 26. The second factor namely anoxemia, comes from failure of either ventricle or both and so may complicate the pulmonary reflex factor when the right ventricle fails in mitral stenosis, the first factor namely that due to pulmonary engorgement, is actually decreased and the second factor may change but little one way or the other since it can be caused either by pulmonary stasis or by peripheral systemic stasis.

Secondary causes of dyspnea superimposed upon the primary factors are most commonly effort and excitement, including the very effort of dyspnea itself which thus starts a vicious circle, cough, nightmares or other sudden fright, paroxysmal tachycardia or atrial fibrillation, pressure from hydrothorax or ascites, and infections and operations.

At first cardiac dyspnea comes only on moderate exertion, but as the degree of failure of the left ventricle increases it comes on slight exertion and finally even when the patient is absolutely quiet. Besides exertion, position is an important factor in the production of dyspnea in advanced cases. There are four reasons for this. When the body is recumbent the blood flow through the heart is greater than in the upright position. It has been reported that the effect of gravity in the upright position relieves the heart of a considerable amount (estimated at about one fourth) of the blood which circulates through it

when the patient is in the recumbent position this reduction of work is important in giving the heart some rest. Secondly and similarly the lungs are also less engorged in the upright position. Thirdly in the upright position there is more room for breathing and free heart action with the diaphragm lower and the pressure from a large liver and ascites less disturbing. And, fourthly in the recumbent position the respiratory center is itself directly acted on by the stasis of the venous blood in severe cases, which gravity in the upright position at once helps to correct so far as the respiratory center is concerned. The symptom of difficult or impossible breathing in the recumbent position is called *orthopnea.*

An important and interesting symptom of heart failure, not always recognized as such, may be *insomnia* due to an ill-defined orthopnea, in such instances, treatment directed to control congestion is likely to be much more effective than the administration of hypnotic drugs which, in large dosage, may result in mental confusion (Wheeler and White, 1945)

There is one very important and striking type of dyspnea of cardiac origin due to acute failure of the left ventricle coming on mostly in recumbency at night but also at times on effort in the daytime. This is *acute paroxysmal dyspnea* which may or may not be attended by signs of pulmonary edema or by an unusual respiratory reflex resulting in asthmatic breathing. When asthma complicates this phenomenon of paroxysmal dyspnea due to sudden pulmonary vascular engorgement the condition is called *cardiac asthma.* Paroxysmal dyspnea due to acute failure of the left ventricle is always serious and sometimes fatal (from the associated pulmonary edema or state of shock) but there is another as a rule less grave cardiac cause of such dyspnea, with or without cardiac asthma, namely mitral stenosis. In cases of marked mitral stenosis a sudden moderate or marked tachycardia, as from the onset of atrial fibrillation which is so common in mitral stenosis, tends to flood the lungs due to overactivity of the right ventricle, and the respiratory distress is precipitated. Pulmonary edema due to mitral stenosis can be very serious (see Chapter 26)

Cough and expectoration with sputum which may be blood-tinged are frequent with edema of the lungs, interstitial and alveolar

Finally so far as disturbed breathing is concerned, there is one other type, not so much dependent on myocardial weakness and congestive heart failure per se as on faulty circulation in the brain itself as from marked cerebral arteriosclerosis or other cause for depression of the respiratory center This is *Cheyne-Stokes respiration* with its waxing and waning of activity of the respiratory center (see Chapter 3) In well-marked cases periods of apnea and hyperpnea of 20 to 30 seconds duration alternate with each other When Cheyne-Stokes respiration occurs in waking hours it is a very serious sign of circulatory failure.

Other symptoms of congestive heart failure are less common than dyspnea and are due in the main to failure of the right ventricle. There is frequently *discomfort from congestion of the liver* more particularly if the liver engorgement is acute, along with tenderness in the right hypochondrium. Actually

the very first symptom of right ventricular failure is liver pain on effort due to acute congestion, much as dyspnea from pulmonary congestion is the first symptom of left ventricular failure it is not, however so impressive (Boyer and White, 1942) Also ascites may produce disagreeable pressure sensations, and edema of the legs may be painful.

Pain is not common in the precordial or substernal regions, but there sometimes is a more or less constant ache in nervous persons with big hearts. Weakness is common but not uniform. Insomnia, headache, nervousness, mental disturbance, and indigestion (the last from congestion of stomach, liver and intestines) are frequent. In a cardiac patient insomnia should always be investigated as being the possible result of dyspnea digitalis may dispel it more readily than hypnotics. Palpitation is rare, unless there is a complicating disturbance of rhythm.

Fever has sometimes been attributed to congestive heart failure and explained as the result of the inability of the skin, because of the edema and disturbance to the peripheral circulation, to get rid of excess body heat. Such upset of the heat regulatory mechanism of the body may perhaps account on occasion for one degree (F) of fever but fever of any significance, that is, of two degrees or more, has been found to be due always to some complication, particularly pulmonary infarction pulmonary infection, or rheumatic fever (Kinsey and White, 1940)

Signs. The chief signs of congestive heart failure are those of blood stasis edema and cyanosis (see Chapter 4 for full discussion of these signs) Circulatory stasis may be primarily in the lungs, due in the main to left ventricular failure, or in liver and dependent parts of the body due characteristically to failure of the right ventricle, or it may be evident in all three circulations—pulmonary portal, and systemic. An important factor which greatly favors the accumulation of fluid in the body in congestive heart failure is the faulty renal function due to inadequate circulation to the kidneys, this results in the retention of sodium and water (see Chapter 4)

In the *lungs* the stasis shows itself first by decrease in vital capacity (Chapter 10) due to decrease in the air space, often also by emphysema (the lungs being distended) and later still by moist rales, beginning at the lung bases and extending throughout the lungs.

In the *systemic circulation* the stasis shows itself by engorgement and visible pulsation in the neck (jugular) veins with the patient upright, by increase in size of the feet and legs, developing into pitting edema, and eventually by an extension of edema to thighs, hips, genitalia, abdominal wall, thoracic wall and infrequently even to the arms and face. Generalized edema is called *anasarca*.

In the *portal circulation* stasis is shown by engorgement of the liver and by stasis distal to the liver The liver may increase enormously in size, so that it reaches the level of the umbilicus, or even lower in a few cases the stomach and intestines are involved also, becoming congested and disturbed in function. *Ascites* is found in the more severe cases. The degree of portal stasis is

often out of proportion to that of stasis in the systemic circulation, due probably to the greater degree of obstruction to the blood flow from the hepatic veins than to that in the inferior vena cava, combined with a high degree of permeability of the capillaries of the portal system.

Even though there is marked portal stasis with engorgement of the liver, jaundice is found in congestive heart failure only rarely When it does occur other factors are responsible, in the main acute or chronic liver damage or extensive hemolysis (as from pulmonary infarction the blood pigment from which the congested liver is unable temporarily to handle) Tests, as with Bromsulphalein, may demonstrate reduction in liver function during acute or chronic congestion

The accumulation of fluid in the pleural cavities (*hydrothorax*) and rarely in the pericardium (*hydropericardium*) is a further sign of congestive heart failure. It is more common in the course of stasis in the systemic circulation to find hydrothorax in the right than in the left pleural cavity (McPeak and Levine, 1946 White, August, and Michie, 1947) The exact explanation of this localization is not clear: it is probably due to greater stasis in the right pleural circulation than in the left either through engorgement or compression of the azygos vein, or because the pulmonary circulation in the right lung has a greater height to travel to reach the left atrium than has that in the left lung, especially when the patient is inclined, as so often happens, to lie on the right side, or because of both these factors. Only a part of the left pleural circulation is drained into the vena azygos major by the vena azygos minor the balance emptying into the left innominate vein, the flow in which is probably obstructed less than in the azygos veins. When the fluid increases in the right pleural cavity it begins to appear also in the left, and finally fluid is found even in the pericardial sac in cases with marked anasarca.

Cardiac enlargement, often marked in degree and sometimes acute (due to dilatation) is always evident with congestive heart failure. Frequently murmurs are found, due either to organic valve disease or to functional valvular insufficiency The heart sounds may be unaffected, but occasionally they are of poor quality due especially to the weakness of the first sound at the apex, so that with tachycardia there may be a so-called tic-tac character to the sounds. Now and then with marked ventricular dilatation there is heard the ominous protodiastolic gallop rhythm, maximal at the apex in left ventricular weakness and at the lower end of the sternum in right. Arrhythmia is frequent but is just as often absent, the chief types are ventricular premature beats and atrial fibrillation.

Accentuation of the pulmonary second sound often reflects the increase in pulmonary blood pressure when the left ventricle fails.

Blood pressure studies with congestive failure show great variations. There may be extreme hypertension, lesser grades of hypertension, normal pressure readings, or hypotension, the last being especially significant of cardiac weakness if there has been a rapid or steady fall of pressure to a low level or even a "normal" level from a previously high level One sign of the greatest im-

portance, usually discovered in the course of sphygmomanometry but often carelessly overlooked, is alternation of the pulse frequently found as evidence of left ventricular fatigue even before the onset of frank congestive heart failure (see Figure 33 page 162, and Chapter 8)

Roentgen ray studies are not of great importance in congestive heart failure, but they do help to determine the degree of cardiac enlargement, especially if there is changing size as in a few cases with acute dilatation (with coronary thrombosis and acute rheumatic carditis, for instance) they also help to show by the heart shape the type of lesion present, and they afford useful information about congestion of the lungs (engorgement of the lung hilus shadows—see Figure 149—and in extreme cases even pulmonary edema) and about the presence and the degree of hydrothorax. Finally fluoroscopy sometimes reveals the weak cardiac pulsations that may accompany failure.

Graphic records are of some importance. The arteriogram may show pulsus alternans, especially after premature beats, the phlebogram (jugular pulse tracing) often shows stasis by the combination of the *c* and *v* waves, and the electrocardiogram may reveal some serious degree of intraventricular block or *T* wave change, findings which are helpful in prognosis. The electrocardiogram, furthermore, quickly gives information about arrhythmias and atrial action, and it is frequently a useful guide in the course of treatment, changes in the *S-T* segment and *T* wave (see Chapter 9) and in the ventricular rate (in atrial fibrillation) affording a control of digitalis therapy The *QT* interval, which is a measure of ventricular systole, is prolonged in congestive heart failure and shortened by effective therapy consisting of digitalis or other measures such prolongation is probably to be ascribed in large part to the attendant cardiac enlargement, chiefly dilatation, for digitalis does not shorten systole in normal persons (White and Mudd, 1929 Phang and White, 1943)

The basal metabolic rate is somewhat elevated with congestive heart failure, even to as high as 40 per cent above normal in a few cases the reasons for this elevation, if thyrotoxicosis can be ruled out (which is usually done easily) are that dyspnea and cough are often present to increase the work of the body even though the patient is in bed, and the myocardium itself as the result of its increased bulk and inefficiency is consuming much more than its normal share of oxygen. The blood is not remarkable. With considerable renal stasis the urine more or less regularly contains albumin and casts and is decreased in amount (oliguria) and renal function tests may show marked renal insufficiency for example the phenolsulfonphthalein, or red," test may give readings as low as 10 or 20 per cent in two hours with delayed appearance of the dye in the urine, compared to the normal two hour excretion of 60 to 70 per cent and rapid appearance of the dye. Also the congested kidneys are unable adequately to excrete salt. With restoration of myocardial sufficiency the urine tends to clear and renal function shifts toward normal.

The rate of the circulation is slowed in congestive heart failure, through the lungs in left ventricular failure and through the systemic veins in right. Thus a delay in the arm-to-lung time from the normal average of 6 seconds to a

reading of 12 seconds, as determined by the injection of ether (see Chapter 10) indicates congestion in the systemic venous circulation, the most common cause of which is right heart failure. If the arm-to-lung time is relatively normal



FIG. 149 Roentgenograms of the thorax during left ventricular failure and following recovery therefrom. Note abnormally large heart and pulmonary edema in *A*. Its clearing of the pulmonary edema and decrease in heart size after 9 days of treatment in *B*. M.B., female, age 44 with hypertensive heart disease (B.P. 190 systolic and 1?? diastolic)

but the arm-to-tongue time is delayed from the normal average of 12 seconds to a reading of 24 seconds, as determined by the injection of Decholin (or other test substance—see Chapter 10) we have evidence of considerable congestion in the pulmonary circulation commonly ascribable to left ventricular failure or mitral stenosis but not to pulmonary disease per se or to bronchial asthma. Thus in doubtful cases of congestive failure, and particularly in distinguishing between pulmonary and cardiac causes of dyspnea, these circulatory rate tests are of considerable value.

The output of blood by the heart is decreased and the volume of circulating blood is increased in congestive heart failure, both values returning to normal on recovery

Exercise tests of various sorts have been recommended to determine the presence and degree of congestive failure the amount of dyspnea and persistent tachycardia and hypertension after stair climbing, walking, running, weight lifting, or respiratory tests have sometimes been considered as criteria of the sufficiency of the circulation. As outlined in Chapter 10 these tests are of but limited value, measuring as they do physical fitness as a whole, rather than cardiac strength in particular The determination, by inquiry or observation or both, of the patient s reaction to the usual demands of his or her own particular daily life is easier less harmful, and more accurate and instructive than is judgment of the heart condition by special exercise and respiratory tests.

Finally there is one further method of study of some value, rather in following the condition of a given case with congestive heart failure already present than in determining its presence in the first place. This method is the measurement by spirometer of the vital capacity of the lungs (amount of air that can be expired after the greatest possible inspiration) The amount of the vital capacity normally about 4 to 5 liters in the male and 3 to 4 liters in the female, varies inversely with the amount of congestive failure, provided other factors, such as inexperience in the use of the test and changing pulmonary disease, do not enter in. Starting at 0.5 to 1 liter during a period of marked failure, the vital capacity may increase rapidly or slowly almost to normal when dyspnea is dispelled by rest, digitalis, and diuretics. To determine the presence of congestive heart failure in the first place, vital capacity studies are less useful than other methods, in particular history taking.

Course and prognosis. Although congestive heart failure is always important, its course and prognosis vary tremendously with other factors. Thus, contrary to some impressions, it is not enough to know that the heart is unable to maintain a sufficient circulation it is, as I have emphasized before, important and often essential to know what conditions are causing the myocardial insufficiency in order to render a reasonable prognosis and to outline the best plan of treatment. For example, slight congestive failure due to chronic hypertension or mitral stenosis may be easily controlled for many years by moderate restriction of activity and digitalis therapy while congestive failure, slight at first but rapidly increasing, with syphilitic aortitis and aortic regurgitation or with coronary occlusion demands a far graver prognosis, life often lasting but

a few months to a few years at best, with much more restriction of activity and in the case of syphilis with the need of specific therapy if the cardiac condition allows. There are many variables in judging congestive failure—speed of onset, severity underlying cause, age of the patient, response to treatment, and the faithfulness of the patient in maintaining the necessary treatment. Every case must thus be considered individually from all points of view and after careful and complete study A snap diagnosis of cardiac insufficiency by a history of dyspnea and by observation of cyanosis and engorged veins in the neck is inadequate it is based on but a small though important part of the situation, the end result of serious heart disease and heart strain. A detailed prognostic analysis of congestive heart failure has revealed that marked cardiac enlargement, old age, and the presence of the more serious uncontrollable precipitating factors and complications are the most unfavorable findings (Boyer Leach, and White, 1941)

To estimate an average duration of life after the onset of congestive failure is misleading because of the great variations that exist, but the severity of the condition in general is shown by the fact that such an average is but a few years Many old persons have dyspnea, the first evidence of congestive failure, for many years without desire or need of seeking medical advice, and the fact that such cases frequently are not included in statistical studies makes any estimate of duration of life after the onset of congestive failure very difficult.

There is, however one condition in the course of congestive heart failure that carries with it a serious and sometimes rapidly fatal prognosis. That is paroxysmal dyspnea with or without cardiac asthma life often lasts but a few months and at best but a few years after the first attack, except rarely but life can undoubtedly be much prolonged by adequate therapy especially digitalization and limitation of physical strain.

Death in congestive heart failure rarely comes from the failure alone but is almost invariably due to some last straw most commonly pulmonary infarction or infection, which may be difficult to diagnose ante mortem.

Complications. The complications of congestive failure are varied the congestive failure itself is a frequent complication of many conditions already noted. Circulatory stasis disturbs the function of many organs lungs, liver stomach, intestines, kidneys, and brain. Undoubtedly the coronary circulation is also often interfered with, to aggravate still further the myocardial weakness. Engorgement of the pulmonary circulation and edema of the lungs not only are a menace to life through asphyxiation but so affect the lungs themselves that they are easy prey to extensive hemorrhagic infarcts on the occasion of pulmonary embolism which is one of the most common and important complications of heart failure, arising as it does from phlebothrombosis due to stasis in the legs (see Chapter 28) Chronic stasis in the liver can lead to atrophy and compensatory hyperplasia, with the end stage of cirrhosis in some very chronic cases of mitral stenosis (and constrictive pericarditis) Gastric stasis predisposes to ulcers of the stomach, and intestinal stasis to chronic indigestion and emaciation and to hemorrhoidal venous engorgement. Renal

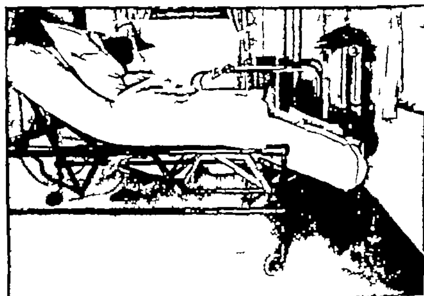
stasis can cause albuminuria, renal insufficiency nitrogen retention, and even rarely uremia. Splenic stasis is apparently less important. Congestion of ovaries and testes may cause decrease in function, sterility miscarriages, and disturbances of menstruation (amenorrhea, menorrhagia, and metrorrhagia) Massive edema of the extremities may result in ulceration of the skin and infection. Cerebral edema and insufficient circulation can cause a sluggish mental state and even delirium and coma in old persons who have narrowed arteries, if they have already a tendency to an unstable mentality Finally terminal infections, particularly pneumonia, are common in the weakened condition of patients with congestive heart failure.

Treatment. The treatment of congestive heart failure may be conveniently divided into seven parts as follows (A) rest, (B) use of digitalis and allied drugs, (C) diuretic drug therapy (D) use of other drugs, including cathartics and hypnotics, (E) the regulation of diet (salt and fluid intake) (F) other therapeutic measures, including venesection, and (G) environment and other factors. Attention has already been called to the fact that in a case of congestive heart failure it is not enough simply to treat the failure it is essential from the standpoint of intelligent treatment to discover when possible, what is back of the failure, as, for example, thyrotoxicosis.

A. Rest and exercise. The two most important remedies that we possess for the relief of congestive heart failure are rest and digitalis (or strophanthin) therapy All other measures, though occasionally lifesaving and often useful, are in general far less valuable. The amount of rest to be prescribed depends on the individual case. For patients who have dyspnea on moderate exertion only there need be merely slight restriction to avoid the exertion which produces symptoms; sometimes, however a period of a few weeks of complete rest is wise in such cases to build up reserve strength and to prolong life. It is necessary to differentiate carefully in such mild cases between the dyspnea of heart failure and that of poor general physical condition or neurocirculatory asthenia, when more exercise rather than less may be advisable. Also it is important usually to allow a patient with heart disease but without failure to take as much exercise as he reasonably and safely can with periods of rest as needed, because it is physical exercise that helps to maintain a state of general good health undoubtedly the proper functioning of the peripheral circulation and of the diaphragm resulting from reasonable exercise aids the heart in its work. The most practicable exercise is walking and this is also uniformly satisfactory: it can be graded easily by three factors—distance, speed, and slope (hill climbing) Other mild exercises like easy golf and croquet may be encouraged at times.

When there is a definite amount of congestive failure at rest or on very slight exertion, exercise, including sexual intercourse, must be prohibited, and absolute rest, at least for a few days, should be prescribed. This rest should not be maintained recumbent, for as already stated, the recumbent position is not a restful one so far as the heart is concerned. An upright or semiupright position in comfortable chair or adjustable bed is the best arrangement for

obtaining the full benefit of absolute rest, a special cardiac bed, such as that shown in Figure 150 is particularly helpful, for it is larger and better adapted to prolonged rest treatment than a chair and also permits ample opportunity



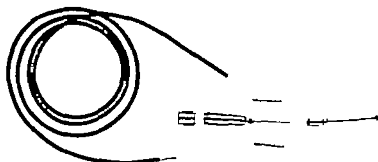


FIG. 150. Photograph demonstrating the treatment of congestive failure by the "Lawson-T [illegible]" cardiac chair-bed (Lewis) and by Southey tubes. The bed is shown with the head partly raised and the foot partly lowered about midway between the possible extreme positions of flat bed and chair. The Southey tubes are inserted in both legs or feet (usually two tubes in each) so that they drain edema fluid by gravity into bottles at the foot of the bed (the bottles may be placed in containers fastened to the foot of the bed) Penicillin is given to prevent infection during their use. The tubes have small holes or slits through which the fluid passes by capillary action from the subcutaneous tissue into the fine rubber tubing. A trochar the handle of which holds the tubes when not in use, is employed to insert the tubes vertically to the skin and subcutaneous tissue up to the cuff over which the rubber tubing fits. The trochar and tubes are reduced to [illegible]/5 natural size.

for changing the patient s position easily There is a great difference between ordinary rest in bed and absolute rest, and this difference may mean the dif ference between failure and success in the treatment of serious congestive failure. With ordinary rest in bed the patient moves about a good deal by him-self, reaches for various things, feeds himself holds a book to read, some times writes or dictates, and often entertains visitors. With absolute rest he does as little as possible himself and is very carefully nursed he is lifted to different positions, is fed, is not allowed to reach for objects or to hold them, to read, or to write he is denied all but a very few visitors of calming and pleasing influence the stimulating effect of noises is reduced to a minimum to while away some of the waking hours, entertaining, light, and restful liter ature may be read to him for short intervals all business and family cares are banned. It is not always easy to start such a regime but with full explanation of its nature and purpose and sometimes with the help at first of sedatives, such as bromides, or of hypnotics if needed, the absolute rest therapy may prove a great success. Generally a few days of such treatment suffice, along with drug therapy when improvement is marked, more activity may be allowed. A mild climate is helpful during convalescence.

B **Digitalis**, or foxglove, either the purple (purpurea) or the yellow (lutea and lanata) is one of the most valuable of drugs its intelligent use is a real triumph in the practice of medicine, permitting the accomplishment of results not possible by unaided nature. Up to 175 years ago digitalis, introduced as a medicinal herb and given its name by Fuchs in 1542, had been applied ex ternally as a counterirritant or used internally as an emetic and purge by the medical profession, when used at all. In 1785 Withering formally introduced it in the treatment of edema, having discovered in 1775 that it was one of the ingredients of an herb mixture used successfully in the treatment of obstinate dropsy by an old woman in Shropshire, England. He enunciated clear rules for its use which, however were followed but little during the next century and it has been only during the last generation that its true worth has been appreciated.

Withering, William (1741–1799) Shropshire, England. *An Account f the Fox glove and some f its Medicinal Uses With Practical Remarks on Dropsy and Other Diseases.* M. Swinney Birmingham, 1785

Pertinent quotations from this important volume, including therapeutic direc tions, are as follows

After having been frequently urged to write upon this subject, and as often declined to do so from pprehension of my own bility I am at length compelled to take up the pen, however unqualified I may still feel myself for the task.

"The use of the Foxglove is getting abroad, and it is better the world should derive some instruction, however imperfect, from my experience, than that the lives of men should be hazarded by its unguarded exhibition.

"Fuchsius, in his hist. stirp 154., is the first author who notices it. From him it receives its name of *Digitalis* in allusion to the German name of Fingerhut,

which signifies a fingerstall, from the blossoms resembling the finger of a glove.

"In the year 1775 my opinion was asked concerning a family receipt for the cure of the dropsy I was told that it had long been kept a secret by an old woman in Shropshire, who had sometimes made cures after the more regular practitioners had failed. I was informed also that the effects produced were violent vomiting and purging for the diuretic effects seemed to have been overlooked. This medicine was composed of twenty or more different herbs, but it was not very difficult for one conversant in these subjects to perceive that the active herb could be no other than the Foxglove.

Withering reported 163 cases treated with digitalis, some of which were successful and some not. The dropsies were usually treated successfully while uncomplicated cases of tuberculosis remained unchanged.

Withering noted communications from correspondents citing cases. A letter from Mr Wainwright, a surgeon in Dudley had the following recommendation. "Collect it in a hot dry day when the petals fall, and the seed vessels begin to swell. The leaves kept to the second year are weaker and their diuretic qualities much diminished. It will therefore be necessary to gather the plant fresh every season.

Withering himself proceeded "the more we multiply the forms of any medicine, the longer we shall be in ascertaining the real dose. Foxglove, when given in very large and quickly repeated doses, occasions sickness, vomiting, purging, giddiness, confused vision, objects appearing green or yellow increased secretion of urine, with frequent motions to part with it, and sometimes inability to retain it; slow pulse, even as slow as 35 in a minute, cold sweats, convulsions, syncope, death.

Directions for use "I give to adults from one to three grains of this powder [powdered leaves] twice a day In the reduced state in which physicians find dropsical patients, four grains a day are sufficient.

If liquid medicine be preferred, I order a dram of these dried leaves to be infused for four hours in half a pint of boiling water adding to the strained liquor an ounce of any spirituous water One ounce of this infusion given twice a day is a medium dose for an adult patient, or once in 8 hours, or ½ ounce at a time. About 30 grains of the powder or eight ounces of the infusion, may be taken before nausea commences.

"Let th medicine therefore be given in the doses and at the intervals mentioned above let it be continued until it either acts on the kidneys, the stomach, the pulse or the bowels, let it be stopped upon the first appearance of any one of these effects.

"Inferences.

"I. That the Digitalis will not universally act as a diuretic.

"IV That if this fails, there is but little chance of any other medicine succeeding

IX. That it has power over the motion of the heart, to a degree yet unobserved in any other medicine, and that this power may be converted to salutary ends.

1 *Action of digitalis.* The action of digitalis on the heart is threefold. (a) In the first place it depresses the pacemaking function of the sinoatrial node and also of the atrioventricular node, with the resulting tendency for the heart rate

to be slowed when there is normal rhythm or in rare cases when there is atrioventricular nodal or idioventricular rhythm. This is, in part at least, a vagal effect and may be removed by paralyzing the vagus nerves by atropine sulfate, 1 to 2 mg (1/60 to 1/30 gr) subcutaneously In different individuals there is often a variation of the degree of influence of digitalis on the rate in normal rhythm. When this depressing effect is not very apparent it can sometimes be easily brought out by pressure over the right carotid artery Sinus arrhythmia as well as sinoatrial bradycardia are common results of digitalis action. These effects of the drug on the pacemakers of the heart enter little or not at all into therapy but they should be known for they explain some of the by-effects of the drug action. There are some cases of the Morgagni-Adams-Stokes syndrome due to paroxysmal heart block which is set off when the normal sinus rhythm rises to a rate, say of 80 at which the a-v junctional tissues are unable to conduct the impulses, it may be possible in such cases by the careful use of digitalis to keep the sinus rate below this critical level, without further depression of a-v conduction. In rare cases with large doses of digitalis it is even possible to paralyze the atria altogether or to irritate the atrioventricular node so that it escapes from atrial control and gives rise to a regular independent ventricular action at normal or somewhat elevated rate.

(b) A second effect of digitalis on the heart is on conduction. This occurs all through the heart muscle with increase in the refractory period of atrial and ventricular muscle, so that atrial flutter for example, is converted into atrial fibrillation (Chapter 33) intra-atrial block and intraventricular block (of either bundle branch, generally of slight degree) as evidenced by changes of the *P* and *QRS* waves of the electrocardiogram (Chapter 34) have, in rare cases, been ascribed to the digitalis effect. The most marked and important influence on conduction, however is on the main tract between atria and ventricles, namely the atrioventricular node (of Tawara) and bundle (of His) Various grades of atrioventricular block are easily induced by digitalis, from slight delay in conduction up to complete block in susceptible individuals. Again, the effect is in part vagal, but apparently only in part, for vagal paralysis often fails to obliterate the effect of large doses of digitalis. Vagal stimulation (by carotid sinus pressure) usually increases easily the grade of block already produced by digitalis or brings it out when latent. The effect of smaller doses of digitalis is apparently largely vagal, the heart rate escaping to high levels as the result of sympathetic stimulation from exercise or excitement, while large doses have a direct *nonvagal effect which may be necessary to keep the heart* rate really under control.

It is this depressant influence of digitalis on conduction that explains half the virtue of the drug. It has long been known that there is one type of patient with congestive heart failure especially helped by digitalis therapy sometimes with astounding success this type is the patient who has also atrial fibrillation with more or less rapid ventricular rate. As noted in Chapter 33 atrial fibrillation is at the very first accompanied by a certain degree of atrioventricular block, the ventricles being unable to respond to the atrial rate of 400, more or

less, per minute. This irregular grade of atrioventricular block is quickly increased by digitalis in full dosage and the heart rate falls to normal or even to low figures, with a great increase in the intervals of rest for the ventricles (long diastolic pauses) and usually with coincident striking relief of the symptoms and signs of congestive failure. The reduction of rate of as much as 100 beats per minute which sometimes occurs in such cases, for example from 160 to 60 means sparing the heart muscle an unnecessary and often ineffective amount of labor consisting of 6 000 beats an hour or well over 100,000 beats a day Even a reduction of but 50 beats which is very common, say from a rate of 120 to one of 70 means an omission of 72,000 contractions a day This is obviously a tremendous relief for an overworked heart. There is no wonder that apparently miraculous recovery sometimes results. With atrial flutter digitalis is often very useful in reducing a fatiguing heart rate, for example, from 150 with atrial rate of 300 to 75 due to the increase of heart block from "2 to 1 to "4 to 1" the atrial rate remaining at 300- in atrial flutter however digitalis tends to have another effect already mentioned, namely to convert the flutter into fibrillation by the production of intra-atrial block, with the ventricular rate still well controlled by the drug action on atrioventricular conduction. With normal rhythm this influence of digitalis on conduction is usually but slight and often not evident at all.

(c) A third effect of digitalis on the heart is on contraction In some manner not yet understood the tone of the heart muscle and the completeness of contraction when there are dilatation and failure are much increased by digitalis. These effects in man are far more apparent in cases of normal rhythm with congestive failure than in patients with atrial fibrillation where they may be masked by the effect of the fall in heart rate. It has been sometimes erroneously thought and taught that digitalis therapy is effective only in the presence of atrial fibrillation, in the manner described in the paragraph above. Digitalis is often, though as a rule less dramatically effective when there is congestive failure with normal rhythm. To withhold digitalis from such cases on the mistaken notion that it will be ineffective constitutes an important therapeutic error To be sure, digitalis therapy in the presence of normal cardiac rhythm is not always effective and its success averages below that when atrial fibrillation is present nevertheless it is often strikingly beneficial and sometimes it is lifesaving. The effect of the drug on contraction undoubtedly plays some part also in the improvement of cases of atrial fibrillation under digitalis therapy along with the reduction of heart rate. Even in the presence of atrioventricular block of high grade the increase of contractile power may control congestive failure without any danger though the degree of block should be followed closely and the drug used with great caution if there is any threat of the Morgagni-Adams-Stokes syndrome. The myocardial effect of digitalis is further shown by depression of the *S-T* segments and *T* waves of the electrocardiogram

The effects of digitalis on the rest of the body are varied. As a rule they are absent or slight until large doses have been administered. Some of the effects

are reflex, due to the action on the heart, but some are direct effects on nervous and other systems.

One of the apparent effects that has been noted by several investigators is that on the veins, both systemic and portal, with constriction acting to aid in the return of blood to the heart.

Serious *toxic effects of digitalis* on the heart may occur if overdosage is allowed, but such extreme effects are rare. Atrial paralysis, atrial fibrillation, various high grades of heart block, a coupled rhythm due to ventricular premature beats every second beat, idioventricular rhythm ventricular paroxysmal tachycardia, and ventricular fibrillation have all been induced in man or in animals by massive doses of digitalis. When any of these disorders of cardiac mechanism are found to result from the digitalis given and not primarily from other factors, the drug should be discontinued, for a high percentage (50 to 90 per cent) of the lethal dose has probably been given by the time such disorders are found. It is also of interest and importance to know that vigorous diuresis in a digitalized patient may release enough additional digitalis into the blood stream from the tissues of the body to produce temporary toxic effects.

The earliest and commonest systemic toxic symptoms are malaise, headache, anorexia, and nausea. Later on, vomiting, visual disturbances, diarrhea, and even cerebral disturbances may occur If any of these symptoms are pronounced the drug should be omitted for a while and then resumed with care. It is important always when searching for toxic symptoms to inquire whether there is blurring of vision or disturbance of color vision—in the latter case objects appear usually yellow or green (Purkinje, 1839) Such visual disturbance may be present but not complained of at once, being masked perhaps by other toxic symptoms. Finally there are individual variations in the ease with which digitalis produces toxic as well as beneficial effects, every case must be considered individually

Allergy to foxglove is excessively rare. It has been reported (Cohen and Brodsky 1940) but I have not encountered an instance myself among a good many thousand cases. The patients whom I have seen who have been easily nauseated or otherwise upset by the drug are those who dislike the taste even when coated tablets are used (regurgitation still gives them the taste) or dislike the idea of taking the drug at all, or those who have previously been made sick by it, which is evidence of the wisdom of avoiding overdosage to start with and of the art of persuasion when the drug is badly needed.

2. *Therapeutic indications for the use of digitalis* There are five chief indications of the need of digitalis therapy (a) congestive heart failure, with or without atrial fibrillation atrial flutter or heart block, (b) atrial fibrillation or atrial flutter with rapid ventricular rate, when quinidine sulfate alone is not administered at once (see Chapter 33) (c) obstinate paroxysmal tachycardia or premature beats which may infrequently be abolished by digitalis, (d) as a therapeutic test when it is uncertain whether or not there is a slight degree of congestive failure, as in the case of old persons with slight dyspnea on exertion, of victims of chronic pulmonary emphysema with a higher degree of

dyspnea than is readily attributable to the lung condition alone, and of patients with massive pulmonary embolism and (e) as a means of delaying or warding off heart failure altogether and even perhaps of preventing further cardiac enlargement, in patients with serious chronic heart strain from any cause who already have big hearts. For other conditions digitalis should not be used; much of it has been wasted in the past and many patients with all manner of illnesses have been made at least temporarily miserable by the toxic effects of digitalis with no resulting benefit. The drug should not be used in any way routinely in preparation for surgical operations (unless there is serious heart strain, congestive failure, or atrial fibrillation) in the treatment of surgical or postoperative emergencies and collapse during anesthesia, in the therapy of infectious diseases, or in treating constrictive pericarditis (acute or chronic) in the absence of atrial fibrillation or flutter or neurocirculatory asthenia. The indiscriminate use of digitalis is to be strongly deprecated.

There are no contraindications to the use of digitalis when the drug is really needed except the very rare Morgagni Adams-Stokes syndrome in high-grade heart block (even in such cases there are exceptions—see page 943) and the very rare individual hypersensitivity to the drug action. Complete heart block without syncopal or faint attacks is not a contraindication.

3 *Preparations of digitalis* The ways in which digitalis is prescribed have varied very much with the years. After its introduction by William Withering and for a hundred years or more it was used mostly in the form of the dried leaf and in tinctures and infusions. At the beginning of the present century the tincture and powdered dried leaf were used chiefly Gradually the tincture itself has been largely given up in this country so that pills or capsules of standardized dried leaf have been in current use more or less routinely during the last two decades and have proved a very satisfactory way of giving digitalis. However during recent years, purified active principles and extracts of digitalis derived from the purple and yellow foxglove have come more and more into use and have the advantage of less need of animal standardization and of simple use by weight alone An interesting preparation for investigative purposes has been introduced by growing radioactive digitalis in an atmosphere of radioactive carbon dioxide (Geiling, *et al*, 1949)

In the previous editions of this book there has been considerable reference to cat units and to the use of frogs for the standardization of digitalis. Fortunately in the future, although such testing is still necessary when one uses the whole leaf it will become less and less necessary to refer to such standardization in discussing treatment with digitalis. In the evolution of the improvement of digitalis preparations a generation ago the strict insistence on some method of standardization helped greatly in getting rid of inert preparations on the market (Pratt and Morrison, 1919) Human standardization has been recommended (Gold, et al., 1942) and, as a matter of fact, is actually the best method of all in dealing with preparations in need of testing, despite its practical difficulty and the considerable variations of sensitivity in individual subjects.

These extracts of digitalis more currently in use today include one of the very old *purified glycosides first introduced over a hundred years ago by* Nativelle (1845) This is digitoxin, also called Digitaline Nativelle, Purodigin, and by other trade names. It is an effective preparation almost a thousand times stronger in its effect by mouth than standardized dried digitalis leaf so that 0.10 mg of digitoxin is approximately equivalent to 0 10 gm of dried leaf. It is my experience, however that it is not so strong, and that for the human 0.15 mg of digitoxin is equivalent to 0 10 gm of digitalis leaf. Other *active principles include digitonin, digitalein, digoxin, Digalen and lanatoside* C (Digilanid from digitalis lanata)

One of the chief advantages of these purified preparations is that they can be more readily given intravenously in full strength. Digitoxin, for example, given intravenously has much the same effect as when given by mouth. The method of administration and exact dosage will be referred to below

4 *Method of digitalis administration and dosage* There has been considerable confusion *in the past as to the strength of digitalis leaf in the U.S Pharmacopeia.* To follow the international standard it was necessary to increase the strength per weight of the drug at the time of U.S.P XI (1936) and U.S.P XII (1942) from that of the previous standard of U.S.P X (1926) The result of all this change was that the standard strength of digitalis leaf now as compared with the strength twenty years ago is in the ratio of .85 to 1 00· thus, a grain of digitalis leaf now is equivalent to 0 85 gr of twenty years ago and a dose of 1.5 gr is equivalent to 1.28 gr of the earlier strength. Because of the greater ease of slow digitalization years ago than now one preparation, namely Digitora (Upjohn) has held to the old dosage and consists of 1.28 and 0 85 gr tablets for convenience in routine use, as will be discussed below under dosage. At first when this change in strength took place, there was a good deal of digitalis intoxication because of the failure of the medical profession in general to be aware of the greater strength of the preparations this situation has now been largely corrected.

The methods of digitalis administration are several. The most common and generally useful is by mouth, applicable to at least 95 per cent of all cases needing the drug. Parenteral injections into vein or muscle and rectal suppositories *should be reserved for the very few cases in which the drug is* urgently needed and cannot for some reason be given by mouth.

There are three important aspects in the matter of giving digitalis (1) digitalization, that is, saturation with the drug, (2) maintenance of its effect, (3) testing its value in a given case. Also there are various methods, namely (1) the common oral administration, (2) the infrequently needed intravenous use, and (3) rectal administration.

Digitalization consists in the administration of enough of any digitalis preparation to obtain the maximal therapeutic effect with as little toxic action as possible. Such digitalization may be rapid or slow and by mouth or by vein. Very few patients, especially in these days of more enlightened treatment, require *emergency rapid digitalization.* When this is necessary the intravenous

route is generally the most suitable. However the result may be quite satisfactory by oral medication provided a rapidly acting drug is used. Figure 151 illustrates the speed with which digitalization can be secured within a few hours by intravenous medication with certain preparations, for example lanatoside C or Cedilanid, and ouabain or strophanthin. A dose of 0.8 mg of Cedilanid (1 cc = 0.2 mg) repeated in full or half dosage in four hours if necessary is an effective method of rapid digitalization, 0.5 mg (½ cc solution) of strophanthin or ouabain is also effective and somewhat more rapid in its action. In each case the effect begins in a relatively few minutes reaching its maximum within a few hours the exact time varies somewhat from patient to patient. Digitoxin may also be given intravenously in the initial dosage of 0 6 mg to 1.2 mg or more for full effect, quite rapidly the special advantage of digitoxin is that it can be given in the same dosage also by mouth with somewhat slower but usually satisfactory result in the course of a relatively few hours. Digitoxin when given by mouth is absorbed essentially in toto and, therefore, can be used in uniform doses.

Standardized digitalis leaf in powdered form may also be used for digitalization by mouth. Its strength is about a thousandth of that of the pure digitoxin and, therefore, in the course of twenty-four hours about 1.2 gm need to be given. Since each pill of digitalis is conveniently put up in 0.10 gm (1½ gr) the total amount may be given in the form of 0.3 gm, that is, three pills four times in twenty-four hours or even 0 4 gm at a dose at four hour intervals, thus getting in the full amount in the course of eight hours, which is rapid enough for the great majority of patients needing quick digitalization. The advantage of divided dosage of any of these preparations is that some individuals are very sensitive to the drug no matter in what form it is given. If there are toxic effects after the first, second, or third dose, the later doses may be reduced or omitted. It is important to try to avoid serious toxic effects from digitalis because of the common need for the constant use of digitalis for weeks, months, or years after it has once been given. Happily digitalis is as effective after ten years as it is the first day There is not the acquirement of tolerance to the drug, hence no need of increasing the dosage with the passage of time as in the case of so many other drugs Most of the so-called allergy or sensitivity of patients to digitalis is the physical or psychologic repugnance to the drug following a toxic effect. I myself experimentally took large doses of digitalis over twenty years ago and I still have a strong memory of the disagreeable taste at the time of toxic symptoms from it. Therefore, the one dose method of digitalization is generally to be avoided unless the situation is very critical otherwise, and we are dealing with a large patient who is apparently not hypersensitive to medicines in general.

Preparations of the whole leaf for example Digifolin, are also available for intravenous use and may be given thus in about the same dosage and time intervals as the pills by mouth.

For slower digitalization it is very convenient to use one week's time for saturation with the drug, for example one may prescribe the medicine to an

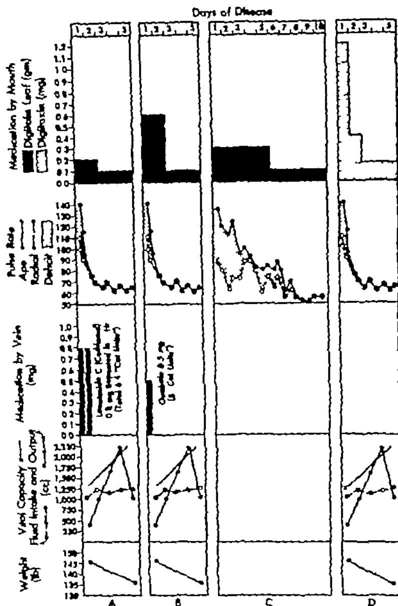


FIG. 151 Charts showing the effects of digitalis in congestive failure and atrial fibrillation, with particular reference to heart rate, clearing of pulse deficit (shown by shading above) fluid balance, vital capacity and weight. (*A*) Rapid effect during the first day of treatment by means of digitalis given intravenously followed by powdered digitalis leaf by mouth. The dosage is indicated on the chart. (*B*) T illustrate essentially the same results to be expected by the use of ouabain intravenously followed by digitalizing dosage of powdered leaf by mouth (see text for comparison of the effects of ouabain and digitalis given intravenously) (*C*) Slower but effective digitalization in a case of atrial fibrillation without congestive failure by powdered digitalis leaf by mouth. Dosage indicated on the chart. (*D*) Effective rapid digitalization of atrial fibrillation by digitoxin given orally

ambulatory patient in hospital clinic or private office and have the patient return in one week to determine the effect. For this purpose the digitalizing dose may be spread through the seven days adding a little extra for excretion each day Thus, if one uses dried whole digitalis leaf of the current strength, one may give a 0 1 gm (1½ gr) pill twice a day for a week or three times a day for four days followed by one pill daily thereafter A few patients need slightly larger doses than this and a few patients slightly smaller but this is the average for the majority of adult patients. If one uses digitoxin, one may give three 0 1 mg tablets daily for a week or somewhat more the first half of the week with maintenance dosage afterward of 0 1 to 0.2 mg. Digitoxin is available in 0 10 0.15 and 0.20 mg tablets. I have found the tablet of 0.15 mg the most suitable of all as a daily ration in the great majority of cases.

There are many other preparations of digitalis which now are all quite satisfactory for digitalization. One of the most useful of all the preparations of the dried leaf is that of Digitora which has kept the old standard strength, a very convenient strength for slow digitalization which, after all, is the best method for the great majority of patients needing digitalization. One tablet of Digitora equals 1.28 gr and can be given three times a day for one week to get just about the right saturation for the average patient, whereas 0.1 gm (1.5 gr) of the current strength of digitalis three times a day for a week is too much for most patients and may induce toxic and, therefore, undesirable symptoms at the end of the week. For rapid or slow digitalization it is possible to give digitalis rectally in the form of suppositories, but these in general are not so reliable, since they are not always absorbed adequately and they are sometimes irritating. Hence this is the least desirable way of administering digitalis, although suitable in rare cases.

A point of much concern in the past has been the question of the dosage with respect to the size of the patient and formerly much calculation was carried out from the standpoint especially of the amount of the drug needed for rapid digitalization. At one time 0 1 gr of the leaf was considered necessary for every ten pounds of weight and although this in general may still hold, there have been so many exceptions to the relationship of the patient's weight and dosage that we no longer bother about such accurate calculation which really is misleading. For a very large person we may rightly prescribe larger doses and for a very small person a decreased dosage, but the wide range of the average between these two extremes does not need to alter what has been written above and what follows below For children the dosage, of course must be less for a child aged 10 to 12 years, half the adult dose is to be advised and for the infant about one quarter

Maintenance of digitalis effect One of the greatest advances in the treatment of heart disease that has occurred in the last generation has been the realization of the importance of the maintenance of digitalis effect. Years ago it was customary to give courses of digitalis with strikingly beneficial effect each time, but with the result that between courses of digitalis there would tend to be a recurrence of myocardial insufficiency and often of severe congestive failure. As time passed, a few individuals became aware of the vital need of maintain-

ing the full digitalis effect in almost all patients who once needed it. Thus we have done away in large part with two common occurrences of the past. The first was the arrival in the emergency wards of the hospitals of cardiac patients with a sudden onset of pulmonary edema or acute distress otherwise due to rapidly developing heart failure or the emergency summoning of physicians to homes or places of work to treat these people. These accidents still occur but, in my experience, they are very much less frequent than they were twenty-five to thirty years ago. Second, one does not see, what one used to, the rapidly recurrent anasarca in patients who, after digitalization, have been allowed to escape from its effect.

For the maintenance of digitalis action there are numerous oral preparations available, the most common and practical being the whole dried leaf itself in tablet or pill form in the dosage of 0.1 to 0.06 gm (1½ gr to 1 gr) daily. Such a tablet or pill may be given daily for weeks, months, or years to maintain the excellent effect as shown by the persistence of a satisfactory heart rate in the presence of atrial fibrillation or by the failure of a return of evidences of myocardial failure with congestion. Some patients need the larger dose and are not made sick by it, others can get along with the smaller dose better and a good many do best with a dosage in between, for example, 0.1 gm (1½ gr) one day and 0.06 gm (1 gr) the next day and so alternately thereafter. Sometimes it is convenient to put up a capsule of 1¼ gr (0.82 gm). Also, conveniently digitoxin can be used for maintenance in the dosage by tablet of either 0.2 or 0.1 or best of all of 0.15 mg daily. Cedilanid may be given in daily rations of an average of 0.25 mg, and digoxin in a daily dose of 0.5 mg. Liquid preparations can still be used although they are much less commonly employed in this country today. The tincture is a reliable preparation of digitalis consisting of a 10 per cent solution. This can be given in a dose of 1 cc (15 minims) corresponding to 0.1 gm of the dried leaf; the dosage of tincture by mouth can thus be calculated readily.

Electrocardiographic control of digitalis therapy is often very helpful. On occasion the electrocardiogram will show definite effects of digitalis action just before beneficial effects become evident and also, on occasion, toxic effects may appear first in the electrocardiogram in the form of bigeminy and marked depression of the *S-T* segments or prolongation of the *P R* interval before they become manifest, as noted above, in the form of nausea, vomiting, intestinal irritation, and disturbance of vision. Figure 152, page 832, shows full digitalis effect in the electrocardiogram of a case of mitral stenosis with atrial fibrillation.

Of considerable interest and importance has been the gradual development of tests of the concentration of digitalis in the blood, one of the most recent of which, a polarographic determination, has been reported by Hilton (1949). It is to be hoped that a routine practical determination may become possible.

Until recently the cost of purified preparations has been so much greater than that of the leaf in powder or tincture form that on the basis of expense many have preferred to continue with the whole leaf. However, as time goes on and costs come down, the purified preparations will be more and more

employed because of the simplicity of the dosage without need of animal standardization.

Finally on occasion it is useful to test the effect of digitalis in any given case where myocardial failure is suspected or where there is some important con-

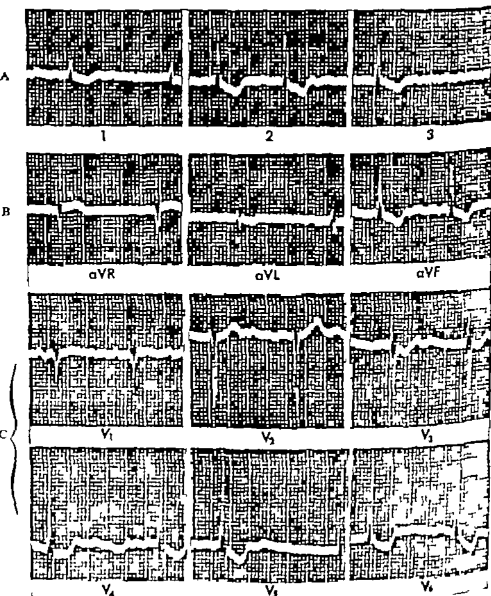


FIG. 152. Electrocardiogram in atrial fibrillation with full digitalis effect, male, age 52. (*A*) Bipolar limb leads 1, 2, and 3. (*B*) unipolar limb leads, aVR, aVL, and aVF. (*C*) six precordial leads, V to V inclusive. Note especially the slow heart rate and the depressed (digitalis) *S-T* segments and flattened *T* waves in Leads 1, 2, 3, aVL, aVF and V to V inclusive. Time = 0.04 and 0.20 second; amplitude 1 mm = 0.10 m

plication that may prevent its full action. The same methods of administration as noted above, that is, of rapid or slow digitalization and maintenance of effect are to be employed, but now and then one may want to use at the start small or moderate dosage without full saturation first. Where the need is not so great, full digitalization is not so urgent, and some benefit may well come from smaller doses, such as the so-called tonic dose of 0 1 gm (1½ gr) or 0.06 gm (1 gr) of the dried leaf daily It is difficult and sometimes impossible to prove or disprove the advantage of this, but there is reason to believe that such "tonic dosage" in the absence of heart failure may help to prevent or delay increasing enlargement of the heart and future failure in cases of constant heart strain as from important valvular disease or hypertension.

There are only two drugs besides digitalis which have digitalis-like action that are of much worth. They are *strophanthin* or *ouabain* and the newly standardized active *glucosides of squill* (called variously as Scillonin and Urginin)

5 *Strophanthin (ouabain)* has been proved effective in emergency treatment but its superiority over an ample intravenous dose of digitalis or its glucosides (digitoxin and lanatoside C, for example) is debatable. However experienced workers with strophanthin clinically chiefly those trained in the continental European and Latin American clinics, report that the drug is superior to digitalis in certain cases for two reasons (1) because of its more rapid full action in emergencies (shown by Eichna and Taube, 1943) particularly when the heart rhythm is normal in acute cardiac failure, and (2) because it is thought to have a greater stimulating effect on a failing myocardium in the degenerative types of heart disease (hypertensive and coronary) Strophanthin or ouabain injected intravenously in the dose of ¼ to ½ mg (1/240 to 1/120 gr) never more, may result rapidly in great improvement with the saving of life or the clearing of the heart failure. The dose may be repeated in 12 hours and then once every day or two as a ration (⅛ to ¼ mg) if necessary but it is better to begin full doses of digitalis by mouth within 12 hours of the emergency injection of ouabain so that the digitalis will become effective at a time when the transient effect of the ouabain is wearing off 0.2 gm (3 gr) of the standard powdered leaf three times daily for two days should suffice before dropping to a ration of 1 or 1½ gr daily It is largely a matter of choice and custom whether one uses digitalis or strophanthin in emergency treatment. On the European continent and in South America strophanthin is often employed successfully while here in the United States digitalis has been preferred. If it seems desirable to use strophanthin, and digitalis has been previously given, an interval of forty-eight hours should be allowed to elapse before the strophanthin is administered intravenously so that danger of poisoning may be prevented.

Strophanthin when given intravenously begins to act appreciably on the heart in a very few minutes (five to twenty) with full effect probably in an hour's time and maintenance of the action for twelve to twenty-four hours. Digitalis given intravenously in potent dosage takes about the same length of

time as strophanthin for initial effect, or perhaps a little longer a definitely longer time for full effect (two hours) and its action lasts somewhat longer (one or two days) (Wyckoff and Goldring, 1927 Pardee, 1928) Digitalis by mouth is slower to act and yet rapid enough in its effect in most cases, showing definite action in two or three hours with full effect in about twelve hours and persistence of action for several days. When full digitalization by mouth has been effected an interval of ten days to two weeks is necessary before all the drug disappears from the system

6 *Squill.* The active principle of squill may be used by mouth advantageously in the very few cases who need digitalis but cannot take it because of a hypersensitive reaction or very strong prejudice against the taste. It is prescribed as scillaren (Scillonin) or as Urginin in tablet form in the dosage of 0 8 mg (1/80 gr) of the former or 1 0 mg (1/60 gr) of the latter as equivalent to 0 1 gm (1 ½ gr) of standardized digitalis.

7 *Other digitalis-like drugs.* Other drugs of the digitalis group, including strophanthus when used by mouth are inferior to digitalis and squill in effectiveness and reliability they include apocynum and convallaria. A newer drug (a cardiac glucoside) with a rather rapid stimulating myocardial effect has been introduced under the name *thevetin,* it comes from the kernels of the bestill nuts of a tropical tree, Thevetia neriifolia, and is related to apocynum; given intravenously it has had in some cases of congestive failure an effect even greater in rapidity than strophanthin (or ouabain) further study of its clinical applicability has been in progress (Arnold, Middleton, and Chen, 1935 Chen, personal communication, 1942, 1949 Modell, et al., 1948)

Very rarely digitalis cannot be taken, even in small dosage, because of its poisonous effect in a particularly hypersensitive individual. It is fair and advisable in such a case to try one after another of the drugs of the so-called digitalis series until one is found that is to some degree effective without being toxic. It may be assumed as a general rule, however that the toxic and therapeutic effects of various preparations of digitalis or of other drugs of the digitalis series are parallel a preparation that can be taken in large dosage without toxic effects is likely to be therapeutically inactive and a preparation that is very active therapeutically tends quickly to cause toxic symptoms. One of the drugs of the digitalis group namely squill, has a reputation as a diuretic, but this reputation is probably based, as is that of digitalis, on inaccurate observation. Its diuretic effect is secondary to improvement in the circulation, there is no primary diuretic action. Finally it is very important to remember that rest alone will frequently give rise to diuresis when there is edema.

8 *Chart of "digitalis" effects.* To follow accurately the effect of digitalis, squill, or strophanthin in congestive failure it is well to keep a careful chart of (1) the apex heart rate and the pulse deficit (difference between apex and radial pulse rates) especially if there is atrial fibrillation, (2) the loss of weight and urine output (as compared to fluid intake) to note a diuretic action, and (3) subjective symptoms of improvement (Figure 151 page 829) The vital

capacity record may also prove of interest, rising with decrease in the degree of failure. And finally the *T* wave of the electrocardiogram often, but not always, shows changes characteristic of the effect of digitalis, becoming diphasic and flattened at first, especially in its early part (or more exactly the *S-T* segment) and eventually with full digitalization becoming deeply inverted (Chapter 9 and Figure 152) When the ventricular rate is high in atrial fibrillation intravenous strophanthin or rapid digitalization usually causes a sharp drop in rate in the course of an hour or two finally in a few hours, there may be complete disappearance of pulse deficit (with even a slight rise of radial pulse rate in rare cases if such radial pulse rate was at first low because of weakness of many of the heartbeats) Along with this remarkable fall in heart rate due to the production of block in atrial fibrillation the electrocardiogram usually shows a rapid change (inversion) in the character of the *S-T* segment, especially in Lead 2. The diuresis that frequently results from digitalis therapy in edematous cases, which, incidentally was the finding that first called attention to the value of foxglove in heart disease, is not the direct effect of the drug but the indirect effect of improvement of the circulation. In the absence of edema digitalis has no diuretic effect.

9 *Miscellaneous drugs without digitalis-like action.* Finally before leaving the discussion of digitalis and other members of the digitalis group, mention should be made of certain unrelated drugs which have been occasionally substituted for or used in addition to, digitalis in the treatment of congestive heart failure because of their supposed stimulating effect on the heart. None of these drugs with one exception, has been shown in any way valuable because of a direct effect on the heart. The exception, *epinephrine* or *adrenaline* has a powerful but transient action. It has not been found valuable in the treatment of congestive failure. At present its chief value rests in the revival of the heartbeat in standstill of the heart, whether because of sinoatrial depression or of high-grade atrioventricular block (Morgagni-Adams-Stokes attacks) it is of less value in the treatment of collapse or shock. It sometimes helps a little in a secondary role in the therapy of an attack of cardiac asthma. A recently introduced drug allied to epinephrine in action but much more gradual and persistent in effect is ephedrine (from the Chinese plant, ma huang) its action in congestive failure is not favorable enough to consider its use even as an extra aid.

All other so-called stimulants, if active at all, produce an effect not directly on the heart but on the nervous system, blood vessels, or other tissues none of them can in any way take the place of digitalis. These drugs include strychnine, camphor caffeine, theobromine and theophylline ethylene-diamine, sparteín, adonis vernalis, physostigmine, crataegus, Cardiazol, Coramine, aconite, and cactus. Caffeine has an important stimulating effect on the nervous system and vasomotor center while Coramine and theophylline ethylene-diamine (aminophylline) often stimulate and regulate a depressed respiratory center and the latter aminophylline, dilates the coronary arteries and dissipates distressing Cheyne-Stokes breathing and the asthmatic dyspnea in acute pul-

monary edema, but they do not so far as we know have a direct myocardial action. Cactus is apparently inert.

C. **Use of diuretics.** When dyspnea (from pulmonary congestion) and edema in congestive heart failure are not quickly relieved by rest, by the effect of digitalis or by diet and fluid restriction, they usually yield to the primary diuretic properties of certain drugs. At times such diuretic drugs are of great importance in maintaining comfort and prolonging life when there is congestive failure. They should be supplementary to and not replace, digitalis, except perhaps in children with congestive failure secondary to acute rheumatic myocardial disease in whom digitalis is generally inert, actually harmful, or at least inferior to such a diuretic as theobromine sodium acetate (thesodate) (Walsh and Sprague, 1941) The diuretics consists of mercury (and bismuth) compounds, purine derivatives, and various salts, including chlorides, nitrates, and urea. The most helpful diuretic drugs which have now come into routine use are the mercurials (especially Mercuhydrin) and ammonium chloride (see below)

1 *Mercury* is a powerful diuretic. It was used for many years in the form of calomel (mercurous chloride) by mouth, but, in more recent years, much more satisfactory mercury compounds for intravenous or intramuscular or even oral use have been introduced. Diarrhea and stomatitis can be very disagreeable toxic effects from the oral administration of mercury although, occasionally astonishing diuresis results. Following the historic use of calomel, there were introduced the newer mercurial compounds, Novasurol or Merbaphen (a mercury-urea compound) Salyrgan or mersalyl (a mercury-salicylate compound) and Mercupurin or novurit (a mercury-theophylline compound) which were given intravenously or intramuscularly in the initial dose of 1 to 2 cc (of a 10 per cent solution) and then daily or at intervals of a few days to one or two weeks or longer in the dosage of 2 cc as needed (Figure 153 opposite) The last two mentioned preparations, Salyrgan and Mercupurin, were more effective and less toxic than Novasurol. The most used mercurial diuretics today are Mercuhydrin (a mercury alluride compound) best given intramuscularly in the dosage of ½ to 2 cc, Mercuranthin (mercurophylline i.e. a compound with theophylline) and Thiomerin (sodium mercaptacetate) this last administered subcutaneously These mercurials can be repeated frequently on occasion, even as often as daily or every other day but it is, of course best to avoid excessive dosage and to increase the interval between injections as soon as possible and as widely as possible. Also, the smaller the effective dose the better Not infrequently ¼ to ½ cc may be quite adequate and not so exhausting as the larger doses of 1 to 2 cc. Care must be used to avoid serious toxic effects, but such are very rare only a few deaths have been reported among hundreds of thousands of injections although true hypersensitiveness to Mercupurin has been noted (Fox Gold, and Leon, 1942) Sodium mercaptacetate (Thiomerin) has the added convenience of subcutaneous administration which makes it possible for personal use by the patient himself or by one of his family

These mercurial preparations may be used with some success even for ascites due to cirrhosis of the liver Extraordinarily large amounts of these drugs have been given to a single patient with constant benefit and apparently no harm whatsoever to kidneys, liver or other organs, for example, 240 cc of Salyrgan in 198 doses to one patient (Maxwell, Scott, and Harvey 1933) and 270 injections over a period of five years to another (Wiseman, 1932) The simultaneous administration of various ammonium or other such salts by mouth often reinforces and increases the diuretic action of the mercury preparations but if they are active themselves there may be no need of giving these other drugs. *Mercury may be given by suppository also, in the form of* Mercurin or Mercupurin, but it is less effective and often irritating.

2. *Bismuth* and *arsenic* though possessing some diuretic properties are inferior to mercury in the treatment of obstinate edema.

3 Of the *purine group* caffeine itself is too weak to be particularly useful. *Theobromine or theobromine sodium salicylate (Diuretin)* is one of the most

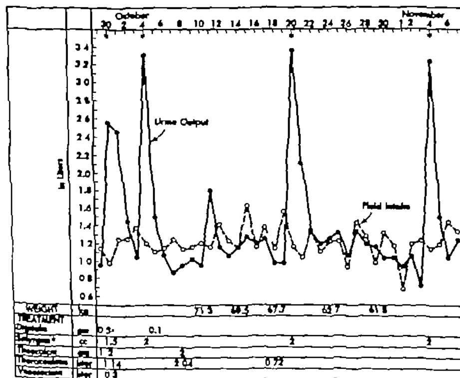


FIG. 153 Chart showing the effect of the diuretic therapy of congestive heart failure in an elderly man. There is especially evident the vigorous action of the mercury preparation Salyrgan (mersalyl) injected intravenously Life was prolonged in relative comfort and quiet activity for about one year in the case of this patient by the occasional use of Salyrgan, digitalization alone with its constant maintenance was inadequate.

* Mercuhydrin, Mercupurin, and Thiomerin may now be used in preference to Salyrgan. (See text.)

valuable diuretics because it is often effective and but slightly toxic. It is best given in the dosage of 0.5 to 1 0 gm (7½ to 15 gr) of the salt, or 0.5 gm (7½ gr) of the alkaloid, in powder or tablet form three times a day for several days or weeks. If effective it may be kept up constantly or it may be discontinued after an interval and then resumed again in repeated courses later for several days at a time, for example, every ten days or two weeks as needed. *Theocalcin (theobromine calcium salicylate)* 7½ gr tablets, or *Thesodate (theobromine sodium acetate)* in enteric-coated tablets of 3¾ to 7½ gr or *Glucophylline* (double salt of theophylline, 1 18 gr and methylglucamine 1 16 gr) may be given in the place of Diuretin. In half of the cases of obstinate edema not yielding to rest and digitalis, theobromine or one of its salts suffices. But for other cases more vigorous diuretics are necessary These include other of the purines, theophylline (or Theocin) and its derivative theophylline ethylenediamine (aminophylline) or Phyllicin, which may be also given for several days trial. If effective, they may be resumed for intervals of a week or two as needed. Either of these drugs, theophylline or its derivative may be administered as small daily rations, in 3 gr doses three times a day but they are more likely to upset the digestive tract than are the theobromine compounds. A more or less constant mild diuresis may be maintained by the use of drugs of the purine group given by mouth

The chief difficulty in the use of either theobromine or theophylline, especially of the latter is that these drugs are very likely to produce toxic symptoms, chiefly nausea and vomiting, but their various salts are much better borne. It may be added that theobromine and allied drugs have been given in the treatment of coronary insufficiency and Cheyne-Stokes respiration, sometimes with great benefit, theophylline ethylene-diamine (Metaphyllin or ammophylline) has been particularly effective in the control of Cheyne-Stokes respiration, given intravenously in the dosage of 0 25 gm (4 gr)—it is always worth trying and sometimes smooths out the breathing within a minute or two.

4 Certain salts, namely *ammonium chloride ammonium nitrate ammonium sulfate magnesium sulfate calcium chloride* and *urea* also have diuretic properties, especially the ammonium salts, associated with their production of a mild acidosis and resultant extraction of sodium from the body When given alone, they may or may not be sufficiently active. In order to produce an effect by themselves they have to be administered sometimes in large doses (for example, 8 to 10 gm of ammonium chloride daily) and they are generally disagreeable to take. As an adjuvant to mercury compounds in the treatment of obstinate edema ammonium chloride or ammonium nitrate is often helpful in the dose of 1 0 to 1.5 gm (15 to 22½ gr) four times daily The ammonium salt should be given in enteric-coated pills of 7½ gr (0.5 gm) each Urea may be given for weeks or months effectively in the dosage of 10 to 25 gm two or three times a day in a 40 per cent watery solution but it is not so useful. Often these salts are not necessary the mercury alone proving adequate but occasionally they are quite effective and worthy of trial when the mercurial therapy is insufficient, and in some cases they may be used alone

with beneficial mild diuresis. Calcium (and potassium) salts (for example, calcium gluconate) in high dosage should not be administered to digitalized patients because of the hazard of serious toxic effects on the cardiac mechanism.

5 Finally, *parathyroid extract (parathormone)* has been found to have diuretic properties. Although it mobilizes calcium in the blood, it acts differently from calcium chloride which causes diuresis by producing an acidosis. Parathormone has not, however been used clinically to replace the other diuretics.

The exact mechanism of the action of primary diuretic drugs is not always clear it apparently is chiefly through the effect of the drugs on the glomeruli (purines) and tubules (mercury derivatives) of the kidneys whether the drugs act also through some process that controls the water content of the tissues themselves is not known.

D Other drug therapy Although drug therapy other than that directed toward rest and stimulation of the heart by digitalis and allied drugs, and that concerned with diuresis, has only a secondary place in congestive heart failure, important effects are occasionally secured which mean the difference between success and failure in a given case.

1 The *narcotics sedatives and hypnotics* are the most important of these other drugs. For acute paroxysmal dyspnea (pulmonary edema) with or without cardiac asthma, morphine sulfate, 0 015 gm (¼ gr) subcutaneously at the onset of the attack has a striking effect to quiet the patient, improve the breathing, and shorten the attack. Also at times a dose of morphine, given to a greatly distressed patient with congestive failure who has been unable to sleep and has been uncomfortable for days, may bring the first rest and peace of mind, and start the patient on the road to recovery morphinism should of course be avoided by omitting the drug as soon as possible. Atropine sulfate, 0 6 mg (1/100 gr) may be given with the morphine to reduce the nausea from its vagal effect, as well as to reduce secretions. Pantopon in the dosage of 0 02 gm (⅓ gr) or Dilaudid 0 002 gm (1/32 gr) may be tolerated better and have as effective therapeutic action as morphine in some patients. Even codeine sulfate may on occasion be used effectively in the dosage of 0 03 to 0 06 gm (½ to 1 gr) subcutaneously or by mouth, in the place of morphine which has more disagreeable after-effects. Bromides, whisky or brandy and the hypnotics (of many kinds) also have a place in certain cases bothered by headache, worry and sleeplessness. Narcotics should be generally omitted when there is distressing Cheyne-Stokes respiration. When phenobarbital and allied hypnotics are ineffective or actually disturbing in their action, and morphine is not applicable, a very useful and safe drug to control insomnia and great restlessness is paraldehyde given by mouth, rectum, or intramuscularly in the dosage of 8 to 16 cc (2 to 4 drachms) to be repeated as needed.

2. *Oxygen inhalation* (50 to 100 per cent oxygen by special mask or in special tent or chamber or by naso- or oropharyngeal insufflation) has an important place in combating dyspnea and cyanosis in acute congestive failure

and in tiding cardiac patients over important complications, especially pulmonary infection and infarction, and, although not suitable for constant use in chronic failure, it may be helpful in daily rations in the case of patients with persistent congestion of the lungs. The introduction of the gas helium in the place of air as the diluent of the oxygen helped very materially in reducing respiratory effort in the inhalation of oxygen (Barach, 1934) but helium leaks easily and has been expensive and difficult to obtain, especially in wartime.

3 In many cases of congestive heart failure or very limited myocardial reserve in which the diet is inadequate or absorption of food elements defective, sometimes because of the disease itself and sometimes because of the effect of drugs, it is essential to administer *vitamins* Such therapy in milder cases may be by mouth in the form of (a) vitamin B complex, which contains thiamine, nicotinic acid, and riboflavin in amounts sufficient to combat beriberi, pellagra, and dermatoses, (b) orange juice to combat scurvy and when necessary (c) vitamins A and D In severe cases with evident avitaminosis, usually multiple, it may be necessary to give vitamins parenterally for example, thiamine HCl 50 to 100 mg daily nicotinic acid 50 to 80 mg, and ascorbic acid 50 to 150 mg or more if needed urgently for actual scurvy (up to 1,200 mg in the first dose)

4 The *cathartics and laxatives* are often indispensable. Half an ounce of magnesium sulfate every day or every other day may yield one or two watery stools which help not only to keep the bowels open but to get rid of edema. Other cathartics may also be used, avoiding those containing sodium. Senna in the form of a simple aqueous extract of the pods is often a mild but effective laxative. Vigorous purgation is to be strongly deprecated because of its weakening effect, which is in part due to the repeated need of going to stool when absolute rest would be far better for the patient, and in part due to the nausea that may be induced.

5 *The drug treatment of other diseases* like syphilis, which complicate congestive heart failure must be carried out with the greatest of care if at all. Generally it is wise to omit all such treatment until the heart has regained its strength.

6 Symptomatic treatment of headache, indigestion, and other functional disorders may be carried out as in the absence of heart failure except that drugs containing sodium should not be given except in very small dosage Various other preparations that have been given in the past for supposedly specific myocardial action like dextrose (glucose) intravenously have been largely abandoned.

E. **Diet, salt and fluid intake.** *Diet regulation* is an important part of the treatment of congestive failure. Much has been written on this subject in the past but practically all the information afforded has been empirical, based on personal or vague opinions about specific foods and fluid intake. General advice has been given to restrict the diet to simple food, relatively light in caloric value and in bulk, with some restriction of fluids and salt. Although this advice has been effective for generations in the case of individuals with heart disease without severe involvement in the form of myocardial or coronary insufficiency many cases have needed better detailed advice. Fortunately

during the last five to ten years such advice has come and, although we are not yet at the end of the story we can be much more specific and helpful, especially in the case of myocardial insufficiency and congestive heart failure.

In the first place, the most important item of all is the *restriction of sodium* to a reasonably low level, sometimes to an extremely low level temporarily to help clear congestion. The specific value of the restriction of sodium chloride in the control of congestion was first clearly pointed out by Widal and Lemierre in 1903 and by Strauss in 1908 It is the sodium that holds water in the body and hence the less sodium intake or the greater the sodium output the less water is held in the body with less congestion and the more comfortable is the patient. There is a limit to sodium restriction, however and sometimes there are unfortunate results in the form of salt lack. Therefore, it is possible to overdo this very helpful therapy of limited salt intake.

Salt, that is, sodium chloride, should be fairly accurately measured in the food and there are tables now listing the sodium content of many foods. The reader is referred to one special list as follows "Sodium and Potassium Analyses of Foods and Waters, Fifth List, October 1947 With Additions and Corrections Mead Johnson & Company Evansville 21 Indiana. The sodium chloride content of the usual diet varies greatly according to individual liking and habit. There is a range from about 5 to 15 or more grams per day 8 to 10 being very common. A simple reduction to 3 or 4 gm a day may suffice to help keep congestion under control. Sometimes, however a stricter reduc tion is necessary to 1 or 2 gm a day and on occasion a stricter reduction is to less than 1 gm which would give an actual sodium level of less than ½ gm. Such is found in certain diets like the rice diet of Kempner Control testing of the amount of sodium taken in can be gauged by the measurement of the chlorides in the urine. Strict sodium restriction can be carried out for a good many weeks or months and in less severe form for years, but there should be frequent appraisal of the details of the diet in each case. Various salt substitutes have been introduced to make more palatable the low sodium diets unfortunately the best, containing lithium chloride, was used too freely and resulted in lithium poisoning in some cases, but in small dosage (a few drops at each meal) it may still be taken to advantage.

An ingenious method for limiting the sodium content of the body has been the administration of resinous compounds which attract and hold electrolytes, in particular sodium, in the gastrointestinal contents (too great a depletion of other electrolytes, especially of potassium, is avoided) various preparations of resin, although not yet perfected and difficult for some patients to take, have permitted the ingestion of more palatable food and longer time intervals between mercurial injections in suitable cases of obstinate congestive heart failure (Dock, 1946 1950)

The next important item about the food and fluids concerns the caloric

It is of interest that John of Gaddesden in his famous book (*Rosa anglica practica medicinae a capite ad pedes*, printed by Johannes Antonius Berreta, Pavia, 1492) refers to the value of limiting the salt content of the diet in cases of dropsy His work was in manuscript at the time of Chaucer in the middle of the fourteenth century six hundred years ago.

value. This should be adequate to maintain nutrition and yet low enough to allow loss of weight if there is obesity Sometimes four or five small meals a day are more readily tolerated than two or three larger ones, especially in the case of a severely ill patient. Not infrequently the old Karell diet (cure de lait) can be used for a day or two with benefit. This consists of 800 cc of skimmed milk divided into four portions during twenty-four hours. This is a starvation diet with restriction of salt and limitation of metabolic needs for digestion which may help to start treatment in the case of a severely congested patient. It is not to be used as a rule for more than a day or two at a time. In some diets such as that of the rice diet the protein intake is very low This is generally not necessary It is usually best to give protein intake enough to keep a normal nitrogen balance—1 gm per kilogram of body weight is usually satisfactory If there is much loss of albumin by the urine in the complicated case, more protein may be added to the food. It is generally best to keep all fats low and to supply most of the calories by carbohydrates.

Finally as to fluid intake, formerly and for centuries as a matter of fact, there was great restriction of fluid intake with unhappy results. The patient was often rendered very miserable and constantly thirsty by the reduction of fluids to one liter or less in twenty-four hours. Now we have come to realize belatedly that adequate fluids should be administered, usually best in the amount of about 2 to 3 liters in twenty-four hours, and in rare cases even more if the kidney status demands such for adequate ridding of the blood of impurities. Only infrequently is it necessary to force fluids. Most patients do well with fluid intake varying from 1½ to 2½ or 3 liters.

In order adequately to control the fluid intake, charts of 24 hour intake and output should be carefully kept during the period of congestive failure and for a few weeks thereafter also so far as possible a daily weight chart should be kept, for often the very first indication of the onset or recurrence of edema is an otherwise unexplained rapid gain in weight.

Vitamins (see page 840) and adequate protein (a minimum of 1 gm per kilogram daily for average-sized adults, amounting to 60 to 70 gm in 24 hours) should be carefully included in the diet in order to maintain as good general health as possible and to prevent complications of avitaminosis and hypoproteinemia which may themselves cause heart trouble and edema, although such complications are not as a rule at all prominent and in severe degree are uncommon, yet they may on occasion be a cause for obstinate edema.

F **Various mechanical therapeutic measures.** 1 *Venesection* is rarely necessary in the treatment of congestive heart failure, but sometimes as an emergency measure it gives relief and saves lives. It was much more often necessary in the days before there was a proper appreciation of how to give digitalis, that is, before the time of more or less universal digitalization and maintenance of digitalis effect, and also before adequate mercurial diuresis and restriction of sodium intake Venesection is applicable to two types of patients first and chiefly the cardiac patient with acute and fulminating congestive failure, as in cases of pulmonary edema and of marked venous congestion, and second,

rarely the chronic plethoric non-nephritic hypertensive cardiac patient who tends to have obstinate or readily recurrent edema and persistently high venous pressure (over 20 cm of water in arm vein) in spite of rest, digitalis, diuretics, and other therapy Blood should be removed from arm vein by knife or needle in amounts between 250 and 500 cc (½ to 1 pt) The procedure may be repeated if needed, but it should not be done unless the venous pressure is elevated and it should not be the first treatment of choice

Another way by which temporarily the heart may be relieved of excess blood especially helpful in acute failure with pulmonary edema, is constriction of the proximal parts of three extremities at a time by blood pressure cuffs or similar bands, cutting off temporarily the venous circulation and so sidetracking much blood. Each extremity should be released in turn for fifteen minutes at a time. *This procedure should, however be used as little as possible because* of the hazard of causing phlebothrombosis in the legs with resulting pulmonary embolism.

2. When rest, digitalis, diuretics, and other measures fail to relieve ascites or hydrothorax, and oppression from the fluid is disagreeable, *paracentesis* should be done and as much fluid as possible withdrawn from peritoneal or pleural cavities, without exhausting the patient. This is especially important in the case of hydrothorax because of the greater embarrassment of the already difficult breathing by the reduction of the vital capacity by the pleural fluid, and because fluid is absorbed more slowly from the pleural than from the peritoneal cavity It is best to use local anesthesia with 0 5 to 1 per cent procaine (novocaine) before the trocar is inserted.

3 For obstinate massive edema of the legs, a condition far less common than a decade or two ago, an incision 3 in. long in the dorsum of each foot or multiple punctures of the skin of each calf may be made to drain off as much fluid as possible aseptically into dressings or sterile jars or pans, but a method much to be preferred is the use of *Southey's tubes* (Southey 1877) small cannulas which may be inserted into the feet or legs by means of trocars, two or three on each side, with rubber tubes to carry off the edema fluid, which can thus be measured (Figure 150 page 8 0) Curschmann s tubes are less desirable than Southey's tubes in the treatment of obstinate edema because of their larger size. It is best to have the patient in the sitting position, preferably in a special chair-bed, to get the full benefit from this procedure. Sometimes enormous quantities of fluid can be drained off by the Southey's tubes, even *as much as 6 liters in twenty-four hours or 15 liters (about 30 pounds) in* three or four days. Painful massive edema of the scrotum which is not relieved by the insertion of the Southey's tubes in the legs may be largely removed by putting one of the tubes directly into the scrotum itself· as much as a liter of fluid can be drained from the scrotum in this way in a day or two. The utilization of these mechanical drainage measures is best reserved, however for cases of obstinate edema which are not relieved in other ways. Infection in such patients can be prevented by the use of penicillin parenterally while the tubes are in use. As indicated above, the need of such treatment has been

steadily growing rarer with improvement of our other therapeutic measures; cardiac patients still fail and die, but as a rule they die dry—we no longer see much anasarca today

4 The method of treatment, a type of cardiolysis, in reality a *thoracolysis* or *rib resection (precordial thoracectomy)* designed to afford mechanical relief to an embarrassed circulation in which heart failure is threatened or has actually begun, which was mentioned in previous editions of this book, has been rarely carried out so far as I am aware. It is similar to the equally rare operative procedure introduced to give relief to the heart when it is tied to the chest wall by pericardial adhesions (Brauer's operation, Brauer 1902) Several ribs and costal cartilages, usually the fourth, fifth, and sixth, of the left anterior chest wall are removed in this operation in order to give more freedom to a very large heart pounding against a rather rigid barrier The operation was apparently beneficial in a few cases, chiefly by relief of subjective discomfort (palpitation and precordial ache) but it must still be considered as an experimental measure and not likely to be helpful in many cases. It has been developed further in the last fourteen years since the publication of the second edition of this book, but it must be realized that there results from this procedure an undesirable deformity of the thorax interfering with the mechanism of respiration.

5 *Total thyroidectomy* in the treatment of congestive heart failure and angina pectoris was an extremely interesting innovation years ago (Blumgart, Levine and Berlin, 1933) It had been observed that a cardiac patient thought to have thyroid disease improved considerably for a period of time after the subtotal removal of a normal thyroid gland this was the forerunner of the idea that was finally put into execution that total ablation might dissipate congestive heart failure and angina pectoris by its effect in reducing markedly the basal metabolic rate and so cutting down the demands on the myocardium and coronary circulation. This idea proved true and the operation became for a few years established as one of the radical measures of cardiac treatment that seemed suitable in about 1 per cent of the patients routinely seen for congestive failure or angina pectoris. Both successes and failures were reported in the application of this treatment. Almost all of the early enthusiasm has waned and yet there remained a place for this idea, and recently it has evolved into a medical thyroidectomy for obstinate myocardial or coronary insufficiency by the ingenious use of irradiated iodine, I 131 (Blumgart and Freedberg, 1948) Minute amounts of this preparation are given by mouth over a period of 2 or 3 weeks in order to introduce from 25 to 100 millicuries into the body a considerable proportion of which settles in the thyroid gland where the cells are exposed to the radiation. In the course of 4 to 8 weeks the metabolic rate is reduced sufficiently to afford relief of symptoms in most cases. A high degree of myxedema is prevented by the administration of small doses of thyroid.

Other surgical operations, such as appendectomy to correct serious lesions in the presence of congestive heart failure should be limited to emergencies, and so far as possible some preparation by rapid digitalization should be

carried out first, if there is inadequate digitalis therapy already Thyroidectomy for thyrotoxicosis is, however one operation which is as a rule indicated rather than contraindicated. This surgical measure may actually abolish the congestive heart failure. In cases of prostatic obstruction also it may be difficult to restore or to hold myocardial competency until the patient has been put on constant bladder drainage and submitted later to a transurethral prostatectomy In any of these surgical procedures the greatest care must be taken in securing the best anesthesia possible (see Chapter 23)

6. *Physical therapy* Special measures of physical therapy—exercises, massage, baths, electrotherapy—have little place in the treatment of congestive failure, except for massage of arms and legs which may be useful in helping to maintain the peripheral circulation and so to prevent phlebothrombosis, the precursor of pulmonary embolism, and gentle passive or active exercises during convalescence but not while there is still dyspnea or edema. Other measures such as carbon dioxide baths and more vigorous exercises are to be prescribed only after the congestive failure has cleared up to help to improve the general circulation and thereby to increase the cardiac reserve.

G. **Environment and other factors.** Finally it is important to remember that a patient may be overtreated and hastened to his end by the too zealous simultaneous application of a number of measures, each one of which may be valuable in itself when applied with common sense. A patient who at home is in a chronic state of slight to moderate but not dangerous congestive failure may be brought for treatment to a hospital, where in a new and strange environment he is bled, purged, much restricted as to food and fluids, and given a number of potent drugs. Unable to stand the strain of so much effective therapy he may die within a few days. *Good judgment* must be well mixed with all the rest of the treatment of such a sick patient as the one with congestive heart failure. Health resorts a long way from the patient's home are far less suitable for his care during severe congestive failure than are hospitals near at hand or the patient's own home itself. During convalescence the change of scene and divers interests at some well-conducted sanitarium or spa may justify the patient's journey thither but good medical supervision should be a requisite: the patient should not return home a wreck as has sometimes happened. Also during convalescence it is worthwhile to prescribe not only graded exercise but some interest, like music, art, science, history literature, or even stamp collecting, as well. Last but not least is the *spirit of cheerfulness* that should surround the patient, a natural attribute of a good doctor and a good nurse and one of the chief elements in the psychotherapy of heart disease.

Differential diagnosis. Congestive heart failure must be differentiated from neurocirculatory asthenia, from the effect of obesity and poor physical training on the respiratory reserve, and from nephritis, starvation, peritonitis, cirrhosis of the liver malignant disease, constrictive pericarditis (acute or chronic) and infections which may cause edema, ascites, hepatic enlargement, hydrothorax, and rales in the lungs. The diagnosis of congestive heart failure is generally readily made by finding the combination of serious organic

heart disease, dyspnea or dependent edema, and a favorable response to digitalis therapy It is particularly important on rare occasions to distinguish acute pulmonary edema due to left ventricular failure or to mitral stenosis from that of so-called neurogenic origin (see page 63 Chapter 4)

There are two conditions that are particularly likely to be confused with the results of myocardial failure, one very common namely *pulmonary disease* and the other rare acute or chronic *constrictive pericarditis* Careful history and physical examination as a rule prevent errors. Pulmonary symptoms and signs are not due to heart disease unless there is evidence of that disease in the form of cardiac enlargement, murmurs of valvular deformity or important myocardial infarction the main difficulty is in determining the relative responsibility in producing symptoms and signs when both heart disease and pulmonary disease are present in the same patient. Acute or chronic constrictive pericarditis causes all the evidences of congestion in the systemic veins, liver and dependent parts of the body that are caused by myocardial failure, but the heart itself is usually but little involved in the case of constrictive pericarditis, except for a rather characteristic electrocardiogram and sometimes a slightly enlarged x ray heart shadow and there is a history usually in a young person, of the gradual development of dropsy especially a big liver and ascites, without adequate heart trouble to account for it and unaided by digitalis therapy· in a few cases an acute pericarditis precedes the chronic trouble (see Chapter 27)

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MYOCARDIAL INSUFFICIENCY AND CONGESTIVE HEART FAILURE

SEE ALSO GENERAL REFERENCES FOLLOWING CHAPTER 2 AND REFERENCES UNDER DYSPNEA AND CARDIAC ASTHMA IN CHAPTER 3 CYANOSIS, EDEMA, AND ASCITES IN CHAPTER 4 GALLOP RHYTHM IN CHAPTER 5 AND BASAL METABOLIC RATE DETERMIN TIONS, FUNCTIONAL TESTS BLOOD FLOW AND CIRCULATION RATE STUDIES IN CH PTER 10

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CHAPTER 31

DISORDERS OF VASCULAR FUNCTION INCLUDING GENERAL VASCULAR FAILURE (SHOCK) AND RAYNAUD S DISEASE

An essential factor in the maintenance of the circulation of the blood is the proper functioning of the arterioles and venules. Disorders of vascular function comprise an important example of the failure of adaptation of the human organism and can have important consequences. They are of two main types (1) general vascular disorders which are likely to be serious, and (2) local involvement of the peripheral circulation as in Raynaud s disease, with little or no influence on the heart itself or on the health as a whole, although at times causing great discomfort. These types together constitute a section of the field of normal and abnormal cardiovascular physiology which is becoming better understood and more clearly defined, but which is still in need of further exploration. As stated in the last edition of this book, neither exact knowledge of the mechanism of these vascular disorders nor their therapy has as yet reached a stage comparable to that of the understanding of disorders of function of the heart itself Although it is certain that knowledge of vascular disorders will gain many additions in the future, as it had indeed already done during the last generation, it is not likely that this chapter will ever become the most important part of a survey of cardiovascular disease as a whole as has sometimes been intimated. The heart perforce remains the most vital part of the circulatory apparatus.

Functional vascular disorders consist of an abnormal degree of distribution of vasoconstriction and vasodilatation and of an abnormal permeability of the walls of the smallest blood vessels. There may be an abnormal degree of vasoconstriction in one part of the body coexistent with abnormal vasodilatation in another part. Just how much the two opposite conditions of vasoconstriction and vasodilatation may be due to local vascular irritability how much to the direct effect of toxins on the vessel walls, and how much to nervous stimulation, central and peripheral, still remains in many cases difficult or impossible to say

GENERAL OR EXTENSIVE DISORDERS OF VASCULAR FUNCTION

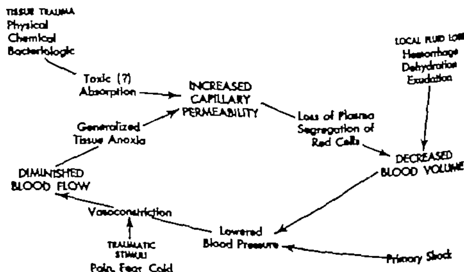
Vasoconstriction. Experimentally general vasoconstriction can be produced by the action of certain drugs, especially epinephrine (adrenaline) and Pituitrin, by direct electric stimulation of the sympathetic nerves, and by indirect sympathetic stimulation by fear excitement, cold, and the toxic condition that causes a shaking chill.

Clinically there is reason to believe that general vasoconstriction, by increasing the resistance to the circulation of blood, is responsible for *essential hypertension* or *hyperpiesia* If such a mechanism exists, as seems likely it yet remains to be discovered whether the vasoconstriction is always due directly to some renal, metabolic, or extraneous toxin in the blood stream to sympathetic nerve effect from central stimulation, or to local irritability of unknown cause widespread throughout the vascular tree. A crystalline pressor substance, called angiotonin, or hypertensin, has been isolated in recent years from the reaction of a renal extract (renin) and renin-activator (Houssay Fasciolo, and Taquini, 1938 Page, et al 1940) Latterly tests of vasomotor lability have been introduced to determine the degree to which generalized vasoconstriction can be influenced and thus judged as to possible amenability to sedative or dilatation therapy or to sympathectomy and also perhaps in picking out potential hypertensive cases These have been called the cold pressor test and the sedation test." They consist of noting the effect on the blood pressure of immersing one hand for one minute in ice-cold water (normally except in very sensitive persons the blood pressure should not rise over 15 mm mercury systolic—Hines and Brown, 1933) and of recording the low levels to which systolic and diastolic blood pressures drop hourly for 1? hours after the administration of 0 2 gm (3 gr) of Sodium Amytal by mouth each time at 7 8 and 9 o clock in the evening (see Chapter 19)

Vasodilatation. Experimentally general vasodilatation can be produced by various poisons and by sympathetic nerve depression. Certain sensitive individuals are more prone to such vasomotor disturbances than are others, and the same person will react differently at different times. Now and than an otherwise healthy young person will faint under the stress of some simple procedure such as the taking of the blood pressure or standing at attention. Also the simple pooling of blood in varicose veins may cause dizziness and other symptoms Extensive vasodilatation may be preceded by a short interval of vasoconstriction.

Vascular shock or failure. General peripheral circulatory failure is a serious state characterized by progressive loss of circulating blood volume due to generalized increase in capillary permeability Two explanations have been advanced to account for this widespread change in capillary permeability first, that it results through the action of some toxic factor absorbed from the area of injury and, second, that the increase in capillary permeability is caused by the tissue anoxia which results from reduced circulation (Freeman, 1942)

Accident, hemorrhage, severe toxemia great pain, and extreme fatigue are all factors which may produce this syndrome of prostration, faintness, hypotension, sometimes coma, marked prolongation of the circulation time, and, in surgical traumatic, and hemorrhagic shock, diminished blood volume. An important secondary infection in the traumatized tissues has been shown to be a cause for a prolonged state of shock (Aub et al., 1944 Prinzmetal, et al 1944) but the prophylactic use of penicillin and other specific measures should protect against this factor in the future A compensatory but unavailing vasoconstriction may be brought into play The following diagram (Freeman, 1942) illustrates the various relationships in vascular shock, which is a process with vicious circle rather than a static condition.



THE PROCESS OF SHOCK

Treatment of milder examples of vascular shock, such as syncope, is simple The recumbent position, rest, inhalation of the fumes of "smelling salts" (an aromatic preparation of ammonium carbonate) a teaspoonful of aromatic spirits of ammonia in a little water a sip of brandy and a drink *of strong hot coffee are all useful procedures in treating faintness of this* sort. Strychnine sulfate given subcutaneously in large doses (1 to 3 mg. 1/60 to 1/20 gr) is thought by some observers to have a favorable effect.

For the more severe cases of "surgical shock, as after severe accident or hemorrhage the treatment is as yet often unsatisfactory *The immediate increase of the volume of the circulating blood best by transfusion is the measure of therapy par excellence* the increase of circulating blood volume by infusion or transfusion is often lifesaving It is best to give whole blood for hemorrhage and plasma when there is fluid loss into the tissues in other states of shock. *Most important of all is the fact that this kind of therapy is far more valuable in prevention when shock threatens than in treatment*

Drugs. The administration of caffeine in large dosage by mouth, subcutaneously or intravenously (10 to 15 gr of caffeine sodiobenzoate) at intervals of three or four hours is only palliative though it may help. Epinephrine (adrenaline) hydrochloride, injected intravenously or intramuscularly in the dose of 0.5 to 1 cc of a 1 1000 solution, and Pituitrin (or the derivative Pitressin containing the active pressor principle with little or none of the oxytocic principle which causes uterine contractions and is used in obstetrics) injected intramuscularly or subcutaneously in the dose of 0.5 to 1 cc (equivalent to 0.1 to 0.2 gr of the posterior lobe of the pituitary gland) have also been recommended for use in shock" but their action is uncertain and likely to be followed by unfavorable after-effects such as increase in the vasodilatation after the transient vasoconstriction, or a primary vasodilatation itself The difficulty with epinephrine and Pituitrin is that they act on the arterioles, whereas the fault lies in the lack of tone in capillaries and venules. Cortical extract has been tried with apparent benefit as a prophylactic against experimental shock in animals and surgical shock in man (Helfrich, Cassels, and Cole, 1942) but its beneficial effect has not been confirmed. Drugs, such as digitalis and strophanthin, directed at the heart itself have proved of no avail and may do harm. The heart in such cases is struggling with an inadequate supply of blood and needs no direct stimulation for itself *it should not be flowed.*

Of late years it has been agreed that *circulatory failure caused by acute infections* should be separated, as to findings and treatment, from that of hemorrhagic or traumatic shock. Ebert and Stead (1941) found in cases of lobar pneumonia with bacteriemia and of streptococcal and staphylococcal septicemia with circulatory failure, characterized by a decrease in peripheral blood flow and a fall in arterial pressure, that measurements of the hematocrit level, serum protein concentration, and plasma volume showed no significant hemoconcentration or diminished blood volume, that the venous pressure was normal, and that elevating the foot of the bed and transfusing with whole blood did not produce any improvement in the circulation. They concluded that the entire cardiovascular system was depressed or damaged by the infection with simultaneous injury to the heart and loss of venous tone, and that therapy must be directed toward overcoming the infection rather than attempting to treat the circulatory failure per se. It may be that shock associated with the acute infections differs from traumatic shock in large part only in the persistence of the exciting factor and not so much in a cardiac factor—which illustrates the need of more light on all the types and mechanisms of what we now call circulatory failure.

The shock syndrome produced by acute myocardial infarction or acute congestive heart failure may need to be differentiated from the circulatory failure secondary to hemorrhage, accident, operation, or infection. When along with signs of diminished peripheral blood flow there is congestion of the pulmonary or of the systemic venous bed, the clinical picture of shock is often to be ascribed rather to the heart failure than to an inadequate venous

return of blood to the heart resulting from decrease in blood volume or pooling of blood in the peripheral circulation (Stead and Ebert, 1942) There are, however cases in which doubtless both factors are responsible, primarily acute coronary occlusion or acute congestive heart failure and, secondarily vascular failure.

LOCAL DISORDERS OF VASCULAR FUNCTION

Vasoconstriction. Experimentally and physiologically vasoconstriction of a single artery or of a group of arteries can be easily induced by direct irritation, by the application of cold and toxic agents to the vessel itself or to the skin over the superficial arteries involved, or by the stimulation of the sympathetic nerves controlling the vessels.

Vascular crises Clinically there are a few abnormal states which are undoubtedly dependent on local vasoconstriction. One of these is the so-called "vascular crisis or spasm, involving cerebral, retinal, coronary or other arteries supplying such vital tissue that important symptoms are quickly produced if the blood supply to this tissue is cut off (Pal, 1905) Transient dizziness, syncope, paralyses, tinnitus, and visual disturbances lasting a few seconds to a few minutes have been commonly reported and thought to be due to local vasoconstriction of somewhat abnormal and irritable vessels; such vascular crises occur for the most part in persons over fifty years of age who have hyperpiesia. It is often difficult to rule out in such cases slight lesions—hemorrhagic, embolic, or thrombotic in nature—but it is quite certain that vascular crises do occur Retinal arterial spasm has actually been observed, and recently it has been proved experimentally that the cerebral arteries are under sympathetic nerve control. Although intermittent claudication (pain in the calves on walking) may in some instances be due to vascular crises, it is more likely that permanent arterial narrowing is responsible there, the circulation being adequate when the muscles are at rest, nevertheless the benefit that sometimes results in these cases from lumbar sympathectomy or procaine injection indicates that there may well be a considerable superimposed vasoconstriction (Freeman and Montgomery 1942) It is possible that vascular crises (coronary spasms) are at times a factor in the production of angina pectoris. When there is a general vasoconstricting storm producing paroxysmal hypertension with or without angina pectoris the condition has been called *Nothnagel's syndrome* (Nothnagel, 1867) This should not include paroxysmal hypertension due to a pheochromocytoma. Also in recent years Pickering (1948) has shown that much of the so-called cerebral vascular spasms constituting a major part of hypertensive encephalopathy is in reality a succession of cerebral vascular accidents (hemorrhage or thrombosis) leaving minute scars of infarction behind them.

Raynaud's disease is a spasmodic vasoconstriction of unknown cause affecting the extremities, usually both hands, often preponderantly either right or left, and rarely the feet. It causes blanching of the skin, a decrease in pulse and symptoms of pain and numbness. The syndrome recurs periodically at

longer or shorter intervals (days, weeks, or months) lasts a few minutes to a few hours at a time, and is induced especially by exposure to cold and to nervous excitement, when severe, trophic disturbances appear and even gangrene may result (Raynaud, 1862) In the late stages the arteries themselves become structurally diseased with thickened walls and narrowed lumina, and in some cases of Raynaud's disease similar changes have been found in the small vessels of the lungs with extensive pulmonary fibrosis (Linenthal, 1942)

Raynaud, M *De l'asphyxi locale t de la gangrène symétrique des extrémités.* Thesis, Rignoux, Paris, 1862.

The following passages from this pioneer work are of interest (Translation by myself.)

From the Preface

"To describe a new disease, and above all to give a new name to group of symptoms which have been long observed and described, is a matter certainly less difficult than to associate several apparently different affections under a common law which controls them.

Moreover in spite of the title which I have given to this thesis, I wish to state at the outset that I have no aspiration to the empty and dangerous honor of pathological innovation. Facts are always but facts, and there is advantage only in grouping them in orderly arrangement.

From Chapter I, page 17

"I propose to demonstrate that there exists a variety of dry gangrene affecting the extremities which cannot be explained by vascular obliteration, variety characterized especially by a remarkable tendency to symmetry to such a degree that it always affects similar parts, the arms or legs, or all four extremities at one time, and even in certain cases the nose and ears also. I shall try to prove that this kind of gangrene has its origin in a defective innervation of the capillary vessels, which will remain for me to describe.

As one can see, this is very restricted corner of the general subject of gangrene which I am now undertaking to discuss.

From Chapter III, page 109

"II. In order to arrange more satisfactorily the symptomatology and to avoid confusing very different conditions because of their serious nature, I shall describe separately local syncope and asphyxia on the one hand and symmetrical gangrene of the extremities on the other

"In its simplest form local syncope is a condition perfectly compatible with good health. Individuals who have this trouble and who are usually women notice that under the slightest influence, sometimes without any appreciable cause, one or more of their fingers grow suddenly pale and cold. In many cases it is always the same finger that is first affected, the others become deadened successively always in the same order This phenomenon is known under the name of doigt mort (dead finger) The attack is painless and lasts from a few minutes to several hours. The provoking cause is often the feeling of cold, what happens ordinarily only under the influence of the most severe cold occurs in the subjects of whom we are now speaking as the result of the slightest drop in temperature sometimes

a simple emotional disturbance is sufficient to produce this effect. It appears that the same cause which acts on the capillaries of the face and produces a blush can, under the circumstances, exert its action especially on the capillaries of the extremities.

"The skin of the affected parts assumes a dull white or at times a sallow shade; it appears completely exsanguinated. The cutaneous sensibility diminishes and then disappears: the fingers become like strangers to their owners. Their temperature drops notably ... The attack is followed by a reaction which is often very painful and which gives rise to a sensation quite like that of a numbing cold in the fingers. ... In cases more pronounced, especially in those with predominant asphyxia, the discoloration of the extremities is replaced by a cyanotic tint of various shades.

Page 129 Ætiology VIII A. Predisposing causes.

Sex This influence is very pronounced in favour of the female sex. Of my 25 cases, 20 were in women and only 5 in men.

Age The influence of age is no less important, and to such a degree that one would be almost tempted to reserve for the condition the name 'juvenile gangrene.' In the great majority of cases the malady appears between the ages of 18 and 30 years, the average of 25 years constituting a time of marked predisposition.

"*Temperament constitution previous illnesses* Although all temperaments are subject to this malady individuals of 'lymphatic' and nervous nature are particularly prone.

Evidence has been published (Lewis, 1929) to indicate that for some unknown reason the palmar arteries are unusually irritable in themselves in Raynaud's disease but other evidence still supports Raynaud's original contention that there is also an important nervous element in the pathogenesis of this disease (White, J C. 1932) Sympathetic ganglionectomy has been carried out in the treatment of Raynaud's disease with definite relief (Adson and Brown, 1929 Mayo and Adson, 1932) It has been reported (Agate, 1949) that a high percentage of workers who polish metal castings with rotary tools show intermittent pallor of their hands.

A form of diffuse scleroderma has been found by Lewis and Landis (1931) to be due to a vascular defect similar to that noted in some cases of Raynaud's disease.

Vasodilatation. Vasodilatation is easily induced locally by the application of heat and by traumatic skin lesions. Exercise of a muscle increases very much the blood flow through it, dilatation of the local arteries and arterioles bringing this about. Sympathectomy temporary paralysis of the sympathetic nerve connections by local anesthetic (as with novocaine) and permanent destruction of the sympathetic fibers by the injection of alcohol cause vasodilatation of the blood vessels in the part of the body affected, and these measures have been employed in the treatment of trophic disorders and of pain which may result from abnormal vasoconstriction

Blushing is a common phenomenon due to local effects on the peripheral arterioles, especially in the face from nervous excitement.

Chronic dilatation of the blood vessels in certain parts of the body *telangiectasis* (τέλος, end ἀγγεῖον vessel, and ἔκτασις development) especially in the face, may follow alcoholism or constant or repeated exposure to the atmosphere of raw climates it is frequently also a congenital defect.

There are two other local pathologic skin conditions dependent mainly on abnormal vasodilatation. These are the common *chilblain*—an acute painful or itching reddened area of skin, usually of hand or foot—due to prolonged exposure to cold and wet, especially in "sensitive individuals, and the rare *erythromelalgia* (ἐρυθρός, red, μέλος, limb, and ἄλγος, pain) of unknown cause, consisting of a paroxysmal abnormal local vasodilatation of the extremities with redness, throbbing, and pain, not usually leading to any trophic disturbance (Weir Mitchell, 1878)

Finally the trauma or toxin that causes local or general vasodilatation may set free from the tissues a histamine-like substance which acts on the walls of the smaller blood vessels, allowing the exudation of fluid into the peri vascular tissues this is most readily seen under the skin in the form of wheals, *urticaria* (from the Latin, *urtica* nettle) (Lewis and Grant, 1924)

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CHAPTER 32

PREMATURE BEATS (EXTRASYSTOLES) PAROXYSMAL TACHYCARDIA

Not much revision has been found necessary in the case of the last three chapters of the book but they have been carefully reviewed to bring them fully up to date.

The commonest and simplest abnormalities of cardiac rhythm are premature beats (or extrasystoles) and paroxysmal tachycardia. Related in mechanism and often occurring in the same patient, they are of but little clinical significance Their frequency and likelihood of overemphasis render them, however a subject of some importance.

PREMATURE BEATS

Premature contractions of the heart, or extrasystoles as they are sometimes called, are due to abnormal or re-entry stimuli in various parts of the heart. atria, ventricles, atrioventricular bundle, and even the nodes themselves. A perfectly satisfactory term is difficult to find. "Premature beat" or "premature contraction" seems most suitable because the chief feature of this abnormality of mechanism is its prematurity· on rare occasions, however when it happens that the normal (sinoatrial nodal) pacemaker is depressed and the normal beat delayed, there may be an abnormal or ectopic beat which is not premature. The term "extrasystole" in common use is less suitable in that the premature beat is only rarely a true extra or additional systole it merely comes early and replaces the normal systole If "extra" is taken to mean "ectopic," that is, arising from an abnormal point, it is more suitably applied, but it is also possible to have a premature beat which arises in or very close to the normal pacemaker

Incidence. The premature beat is almost universal. Probably only a very rare individual escapes having premature beats at some time of his life although they often pass unnoticed. It is without doubt the commonest of all cardiac abnormalities in fact, it is so frequent among otherwise normal individuals that it hardly deserves the name of abnormality

Mechanism (abnormal physiology). A wave of excitation and contraction may arise abnormally in the heart, spreading from a point outside the limits of the normal pacemaker (sinoatrial node) or rarely from within the normal pacemaker itself (and then called *nomotopic*) The stimulus must occur at a time when the muscle will respond, that is, when it is not still in the refractory (unresponsive) phase due to the existence of a state of contraction or recovery It is possible that the premature beat may be the result of the re-entry of the previous normal (or abnormal) excitation wave by way of an area of muscle refractory to the direct spread of the wave but recovering sufficiently to allow response a little later to the same excitation wave reaching it slowly in a roundabout course.

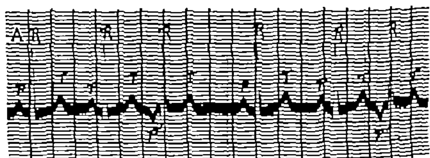
(a) *Atrial premature beat* An abnormal wave starting in the atrial muscle spreads in all directions it not only descends to the atrioventricular junctional tissue, thus giving rise to a ventricular response, but it also ascends to the sinoatrial node, thus discharging a normal impulse already in the process of development, and so interrupting the dominant rhythm. The atrial premature beat, whose atrial component in the electrocardiogram (*P* wave) is usually inverted, is followed by a pause which is equivalent to the time interval needed for its impulse to reach the sinoatrial node plus the usual time interval between two normal sinoatrial contractions. This pause plus the time interval between the normal beat just preceding the atrial premature beat and the atrial premature beat itself gives an interval less than that covered by two normal beats, hence this pause is not "compensatory the spacing of the groups of beats in electrocardiogram and arteriogram is interfered with, and the "dominant rhythm is disturbed (Figure 154 page 868)

Usually the ventricles respond to an atrial premature beat, but often they do so in an abnormal way that is, there is a state of intraventricular block or defective conduction in the bundle branches such block is doubtless due to relative degrees of refractoriness (or slowness of recovery from the previous contraction) in various parts of the conducting system. The earlier the atrial premature beat, the more likely is the ventricular response to be abnormal, that is, to show intraventricular block. Such abnormal response has not been found to be of any clinical significance, as it is a more or less normal, transient, functional condition. Rarely the ventricles may fail to respond at all to atrial premature beats, this lack of response is not remarkable if the abnormal beat comes very early but it is strongly suggestive of some important degree of atrioventricular block if the premature beat is not very early

(b) *Ventricular premature beat* If an abnormal excitation wave starts in right or left ventricle it spreads in all directions sometimes, if it starts very late in diastole, it meets the normal wave as it comes down through the junctional tissues from the atria and produces with it a composite contraction, a condition comparable to that which may also occur in the atria in the case of atrial premature beats.

Usually the premature ventricular wave passes up to the atrioventricular bundle and node but not through it into the atria, the normal atrial contr-

tion begins at this time and thus occurs simultaneously with the abnormal ventricular contraction. The atrioventricular valves being shut as the result of the ventricular premature beat, the blood is deflected back from the atria by the normal atrial contraction into the great veins. Since the premature ventricular contraction does not as a rule disturb the normal regular sequence of atrial waves, it is followed by a pause which is called "compensatory" and the



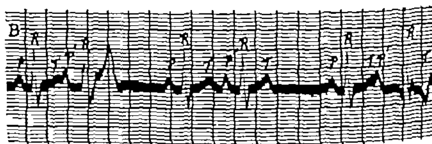


FIG. 154 Electrocardiograms (Lead 2) showing atrial premature beats. (A) Inverted P waves with normal ventricular response, (B) upright but premature P waves with abnormal (aberrant) ventricular response varying in degree according to the prematurity of the P waves.

"dominant rhythm" is not disturbed. The interval between the normal heart beat just preceding the premature beat and the ventricular premature beat itself added to the compensatory pause between the ventricular premature beat and the next normal beat gives an interval just equal to that covered by two normal beats, when sinus arrhythmia is not present to interfere seriously with the measurements (Figure 155)

Sometimes the ventricular premature beat sends its impulse back through the atrioventricular bundle and node to cause a "retrograde" atrial contraction It does then interfere with the dominant sinoatrial rhythm just as an atrial premature beat also interferes with such rhythm When this happens the pause following the ventricular premature beat is not "compensatory" The electrocardiograms of ventricular premature beats are usually bizarre so far as shape of the QRS and T waves are concerned, due to the abnormal spread of the impulse resembling somewhat that in bundle branch block. When the impulse has

its origin clearly in the left ventricle and spreads up and to the right, the *QRS* wave in Lead 1 is wide and chiefly inverted with high *T* wave, and is rather similar to the *QRS* wave seen in normal rhythm with right bundle branch block, when it rises clearly in the right ventricle the *QRS* is wide and upwardly directed in Lead 1 with deep *T* resembling the *QRS* seen in normal rhythm with left bundle branch block, the *QRS* and *T* waves in Lead 3 are almost

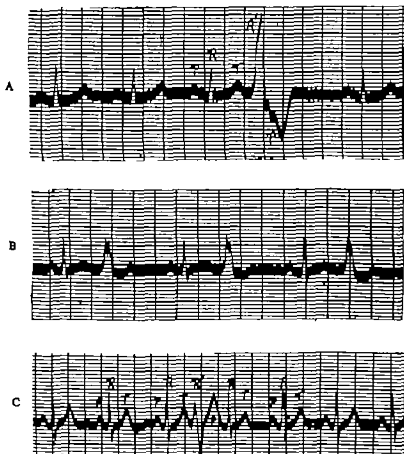


FIG. 155 Electrocardiograms (Lead 2) showing ventricular premature beats (*A*) followed by compensatory pause, (*B*) occurring every other beat to produce bigeminal pulse, and (C) interpolated.

always oppositely directed to those in Lead 1 The precordial leads may pick out the origin of the premature beats quickly both by the short interval before the intrinsic deflection and by the upright direction of the complex over the ventricle involved.

The separation of right and left ventricular premature beats is of little or no clinical significance.

Finally the ventricular premature beat may come so early or the preceding heart rate may be so slow that the ventricular tissue is no longer refractory when the next normal sinoatrial impulse reaches the junctional tissue: the ventricle then responds again in rather quick succession, but usually with some delay due to partial atrioventricular block, and with relatively small pressure because of the small amount of blood left in the heart. Such a mechanism is called "interpolation" of a ventricular premature beat (*Interpolated ventricular premature beat*) and is an example of a true extra or additional systole (Figure 155C)

(c) *Atrioventricular nodal premature beat* A premature beat arising in the atrioventricular node or bundle and causing simultaneous contraction of atria and ventricles has an effect like a ventricular premature beat with retrograde atrial contraction and disturbs the dominant rhythm just as does an atrial premature beat. It is, however a rare type

(d) *Sinoatrial nodal (nomotopic) premature beat* A premature beat may also arise rarely in or close to the sinoatrial node (nomotopic) such a beat acts like an atrial premature beat followed by a relatively short pause, which is in fact just the length of an interval between normal beats.

Parasystole The subject of the mechanism of premature beats should not be left without mention of the interesting theory of parasystole, which helps to explain the regular occurrence of repeated premature beats in certain cases. It is proposed that a new and abnormal pacemaker is constantly building up stimuli just as is the normal sinoatrial nodal pacemaker but at a different rate. When the refractory state of the muscle and local block about the abnormal pacemaker do not interfere, the impulse from the new pacemaker gives rise to premature beats in a regular or irregular relationship to the normal beats. The relative rates of the independent rhythms in parasystole can be worked out by careful measurements of the tracings Whether or not the impulse production in such abnormal pacemaker may be of the character of a circus wave is not known.

Etiology *Cause* The cause of a premature beat is an abnormal stimulus production or course in the heart muscle. Certain factors are sometimes responsible for such an abnormal mechanism, but the manner of their working is obscure. Direct electrical, mechanical, or chemical stimulation of an experimental animal's heart will produce premature beats if the stimulation is of sufficient strength, that is, if it surpasses a certain "threshold" of responsiveness. Nerve stimulation may also induce premature beats.

In man premature beats have been induced by mechanical stimulation (tapping) of the heart exposed either during operation for some thoracic condition or in very rare cases exposed congenitally Electrically induced premature beats have also been reported in the case of a man with heart bared during drainage of a purulent pericarditis (Barker Macleod, and Alexander 1930) Vagus nerve stimulation by carotid pressure in the neck or reflexly by sudden pain anywhere in the body has occasionally elicited premature beats. Forced respiration breath holding, overexertion, and excitement may induce

them. Fatigue, indigestion, cerebral lesions, and hypertension render them more likely or may even cause them on occasion. Certain poisons, infections, and internal diseases are sometimes associated with the appearance of premature beats. Individual susceptibility is an important factor as shown by the induction of extrasystoles in some persons and not in others by tobacco, tea, coffee, alcohol, and certain drugs. Finally heart disease itself favors the occurrence of premature beats and seems occasionally to be a direct cause, but many persons with heart disease do not have premature beats, and vice versa.

Sex. Both sexes frequently show premature beats, the male sex more often, as evidenced by a series of 218 cases of my own with a slight preponderance of males (123 95) (White, 1926)

Age Premature beats may occur at any age they are, however most common (in fact, almost universal) in old age and rare in infancy and early childhood.

Pathology There are no specific lesions of heart or nerves associated with premature beats. Organic heart disease may or may not be present when it is, the myocardium itself is usually normal, except for hypertrophy Given a person with premature beats, the chances are more than ten to one that no significant structural abnormalities of the heart are discoverable. Premature beats are, however relatively more numerous in the presence of heart disease than in its absence; this is probably to be explained by the strain on the heart muscle resulting from some defect like valvular disease, hypertension, or coronary disease.

It is convenient and of some clinical value to separate premature beats into two main groups, namely atrial and ventricular according to their point of origin. Ventricular premature beats are much more common than atrial premature beats, the ratio being about two to one, the ventricular premature beats are less important clinically Atrial premature beats, although often occurring without any discoverable cardiac lesions, are more likely than are ventricular premature beats to be found in heart disease, especially when there is mitral stenosis; they then may be the precursors of atrial fibrillation Premature beats arising in the atrioventricular junctional tissues may be classed with ventricular premature beats so far as their clinical significance is concerned.

Symptoms. There may or may not be symptoms with premature beats. Probably at least one half of all individuals with this arrhythmia are unconscious of its presence, and its discovery in these individuals is an accidental finding on some routine examination. Often, however the occurrence of the premature beat is felt as a more or less disagreeable sensation, due less to the abnormal beat itself than to the pause which follows it, to the vigorous thump of the first normal beat after the pause, or to the pressure wave forced up into the neck veins from the right atrium at the time of the premature beat; this pressure wave results from the contraction of the atria while the ventricles are in systole. The sensation may include two or all three of these elements, but it is rarely very disagreeable.

The occurrence of many premature beats may at first cause much discomfort, but if these beats are continually recurring they tend gradually to lose their irritating character and finally they are scarcely or not at all noticed.

It is, however, true that persons with coronary insufficiency may have painful premature beats for the same reason that such individuals with paroxysmal tachycardia may have a status anginosus during the rapid heart action because of the inability of the myocardium to be properly oxygenated during such short diastolic rests; quinidine may be very beneficial in such cases; this may help to explain its usefulness on occasion in angina pectoris. Sometimes, in hypersensitive subjects, pain may actually be felt with each abnormal contraction and a severe neurosis may result. An erroneous diagnosis of angina pectoris has frequently been made in these individuals; careful study easily prevents such gross error.

When premature beats are so numerous that they interfere with the circulation, as in rare instances when they occur in short series or more often than the normal beats, dizziness and faintness may result, but such symptoms are more likely to be due to an associated nervous reaction. If the premature contractions occur as interpolated beats, that is, between two normal beats without pause, or in short runs, the subject may be conscious of a slight fluttering sensation during the period of the three beats occurring in rapid succession.

Signs. The pathognomonic sign of a premature beat is its prematurity, which may be discovered by auscultation of the heart itself, by palpation of the arterial pulse, by inspection of the jugular pulse, or by the study of graphic records. Feeling the pulse at the wrist is usually the least satisfactory way of detecting the premature beat, for two reasons. In the first place, the abnormal beat is always relatively later in appearance in the pulse cycle at the wrist than at the heart, a weak beat traveling more slowly along the arteries than a normal, strong beat; therefore a premature beat which is but little premature may not be noted as such by the finger on the radial pulse. Secondly, if the beat is very premature and weak it may not reach the radial artery at all or have sufficient force to be felt; the resulting long pause may then be wrongly attributed to partial heart block or to sinus bradycardia rather than to the actual premature beat arrhythmia.

Blood pressure studies show almost invariably a lower systolic and smaller pulse pressure with a premature beat than with a normal beat, and sometimes there may be no measurable pressure at all. Infrequently the premature beat occurs so early that there is not enough intraventricular pressure to raise the semilunar cusps and only a first heart sound is heard, sometimes very faintly coming like a third heart sound or a reduplicated second sound of the preceding normal beat (*frustrane contraction*). Occasionally a considerable pulse deficit (the difference between apex and radial pulse rates) may be found if many very early or weak premature beats occur; the radial rate may be half the apical in bigeminal rhythm.

For complete analysis of a premature beat electrocardiograms are essential; mechanical graphic records of arterial, venous, or cardiac pulsation are he-

ferior Usually it is immaterial to know whether a premature beat is of atrial or of ventricular origin or in what part of atrial or ventricular tissue it arises, and the discovery of premature beats on auscultation of the heart or on palpation of the pulse may not need further detailed study It is well, however when possible, to identify atrial premature beats for they often do presage paroxysmal tachycardia or atrial fibrillation. It is still more important to look for alternation of the pulse that may be revealed by a premature beat and which is of so much greater significance than the premature beat itself (see Chapters 8 and 30)

The differentiation between atrial and ventricular premature beats, in the absence of a phlebogram or an electrocardiogram, lies in the presence or absence of a compensatory pause. This, as a matter of fact, is a very rough and unreliable criterion, even with graphic records of the arterial pulse. Slight differences of time that may differentiate between a compensatory pause and one that is not fully compensatory are difficult or impossible to measure by finger ear or even sometimes by arteriogram. A more important source of error is the fact that a ventricular premature beat may not be followed by a compensatory pause if it induces a backward-coursing, or retrograde, atrial contraction, as it sometimes does, thus breaking up the dominant rhythm. Moreover a ventricular premature beat may be succeeded by atrioventricular nodal escape or by sinus arrhythmia and quickening of rate, which occur occasionally to interfere with the application of the principle of the dominant rhythm. At times, too an atrial premature beat is followed by a pause that is unusually long, either because of succeeding sinus arrhythmia and bradycardia or because the site of abnormal stimulus production in the atrium is so far from the sinoatrial node (for example, in the left atrial appendage) that the time expended in traveling back to the node to interrupt its rhythm and the time between the previous normal beat and the premature beat make an interval that is almost indistinguishable from the usual normal time interval.

The electrocardiogram has the great advantage of revealing the presence and type of a premature beat by mere inspection, usually without the need of any measurement whatsoever the premature beat is almost always ectopic in origin and so it is of abnormal shape in the electrocardiogram. It is possible by this method of study to determine roughly the site of the abnormal impulse in the atria or in the ventricles. For example, a deeply inverted *P* wave usually indicates that the ectopic focus is far from the sinoatrial node and located near the atrioventricular node or in the left atrium, although exact localization is as yet impossible (Figure 154) There are also fairly characteristic shapes for the complexes of so-called basal, or right, and of so-called apical, or left, ventricular premature beats, as already noted above (Figure 155)

Course and prognosis. A few premature contractions of the heart may occur for a short interval of time (an hour or a day) and never return so far as we know or they may come at more or less frequent intervals, once -
once an hour once a minute, or at frequent, often regular intervals, e-
second beat, or very rarely they may be more numerous than the

When they occur every second beat they give rise to a coupled rhythm or bigeminal pulse, or if they are too weak to reach the radial pulse a slow regular rhythm at one half the apex rate is felt at the wrist. When they occur every third beat they cause a trigeminal pulse at the apex and ordinarily at the wrist, or a bigeminal pulse if they fail to reach the wrist. If they are interpolated, there are regular sequences of three beats in rapid succession at the apex and wrist or if the interpolated beats fail to reach the radial pulse there is a pseudo-alternation, every other "normal" beat following the premature beat being late and small. When the premature beats occur every fourth beat they give rise to a quadrigeminal pulse at apex and wrist, or to a trigeminal pulse at the wrist if they fail of transmission.

The premature beat is of no clinical importance except in five respects. In the first place, individuals with heart disease show relatively a higher incidence and greater frequency of occurrence of premature beats than do those with normal hearts, even though the absolute incidence of premature beats is greater in persons without heart disease. Secondly ventricular premature beats occurring every other beat, or in pairs after every normal beat, and those which show by electrocardiogram two or more different shapes and directions of complexes, especially if they alternate in shape and direction, are evidence of a serious toxic or otherwise irritable state of the myocardium and demand careful study and treatment. Thirdly the premature beat is sometimes a source of great discomfort or fear that must in itself be treated. Fourthly painful premature beats induced by effort may prove to be confirmatory evidence of the presence of coronary insufficiency And, finally the premature beat is now and then directly traceable to some toxic substance like digitalis or tobacco, the reduction or omission of which suffices to get rid of the arrhythmia. In the case of digitalis poisoning there may be a bigeminal or coupled rhythm, with or without atrial fibrillation, due to the regular occurrence of ventricular premature beats the appearance of this arrhythmia in the course of administration of large doses of digitalis indicates that a considerable percentage of a lethal dose has been given, probably close to 75 per cent.

The diagnosis and prognosis of heart disease depend not on the presence or absence of premature beats but almost entirely on other evidence of trouble, as Mackenzie so clearly pointed out.

Mackenzie, J "The Extra-systole. Chapter XXVII of *Diseases of the Heart*. 3rd ed., London, 1913 page 199

"Extra-systoles or intermittent heart, as they are sometimes called, occur so frequently and are viewed by the profession so seriously that it is necessary to indicate their bearing on the individual's future. Hitherto their cause has been unknown, and individuals showing them have been considered unfit for admission into the services, military naval, and civil and have been considered unsuitable for life premiums and they have been made miserable for life by the vague prognostications of danger and have been subjected to prolonged and quite unnecessary treatment.

"The fact that the occurrence of an extra-systole is due to some part of the heart's structure being temporarily more excitable than the normal starting-place, has led to the idea that it may be an evidence of some disease process. A certain amount of confirmatory evidence for this supposition is found in the fact that people with undoubted disease of the heart do show extra-systoles, and that extra-systoles have sometimes been found to precede the appearance of grave disturbances of the heart's action, as auricular fibrillation (Case 51). For these reasons, there has been a tendency to view extra-systoles as signs of some gravity. If, however, the subject be studied from a wider and more practical outlook, it will be found that extra-systoles in themselves are not signs of any specific injury to the heart, nor should a prognosis of any gravity be based on their appearance alone. I have watched individuals for over twenty-five years who have presented extra-systoles, sometimes with greater frequency than at other times; and these people have led laborious lives, and have never shown the slightest symptoms of heart failure, or any other evidence of heart impairment. I have had similar experiences with people who have shown all forms of extra-systole, auricular, ventricular and nodal. I have watched young people grow into manhood and lead vigorous lives. I have watched elderly people live beyond 80 years of age, in whom I had detected extra-systoles at the age of 60, and when they did die the cause of death was not primarily cardiac failure. A short time ago, I was consulted by a man, aged 69 years, whom I found in fair state of health. He presented auricular extra-systoles at frequent intervals; and when I remarked upon this he told me that they had been present for over fifty years. Time and again he had submitted to prolonged treatment, without avail, for the purpose of curing this irregularity. He had oftentimes been made miserable and depressed by the grave prognostications of his medical advisers, and had, up to the time when I saw him, been under the apprehension that he had some obscure heart affection which might prove fatal at any moment.

"From such facts as these, that healthy men and women may present this form of irregularity, it can be gathered that extra-systoles in themselves are signs of no significance so far as the efficiency of the heart is concerned.

"It may therefore be stated that when the extra-systole is the only abnormal sign, the prognosis is a favourable one, and where it is associated with other signs the prognosis is to be based upon these other signs.

Treatment. As a rule, premature beats in themselves demand no treatment. Complete reassurance as to their significance can and should almost invariably be given. If there is heart disease or other illness, treatment should be directed toward such disease without regard to premature beats, unless these abnormal beats cause much discomfort in themselves or unless they are evidence of poisoning by something which can be easily controlled. If there is no evidence of any disease and the premature beats do not occasion much distress, reassurance usually suffices to relieve the individual of his fear and much of his consciousness of their presence. It is usually best to tell the patient of the finding of premature beats even when he does not feel them in order to prevent his being unduly alarmed if they are later discovered and taken too seriously by some physician, or if their existence becomes evident to the patient himself.

Often the successful treatment of or the spontaneous recovery from, whatever disease is present suffices to get rid of the premature beats. For example, digitalis, which in full dosage may cause premature beats, may also actually dispel them either directly or as the result of successful treatment of an associated heart failure digitalis, however much more often causes than dispels premature beats.

If some factor like tobacco, alcohol, fatigue or constipation appears responsible for premature beats, or is attended by their presence, control of this factor generally an easy matter may suffice to abolish the premature beats. Operative correction of some trouble such as gallstones has also been known to be followed by a disappearance of premature beats. Usually however no special measures are effective and the premature beats come and go without possibility of their control.

When premature beats are especially annoying and occasion, because of the discomfort they cause, a real state of ill health in themselves, sometimes amounting even to a partial or complete invalidism careful redirection of the patient's mental and emotional outlook should be undertaken and various drugs may also be tried. The six drugs most likely to help are in their order of choice (1) quinidine sulfate, as a 0.2 gm (3 gr) tablet three or four times a day (2) for ventricular (not atrial) premature beats procaine amide (Pronestyl hydrochloride) in the dosage of 0 5 to 1 0 gm (one tablet = 0.25 gm) orally every three to six hours (3) potassium salts, for example, 2 to 4 gm (30 to 60 gr) of the acetate in 25 per cent solution in peppermint water every 4 to 6 hours, especially effective in the case of premature beats due to digitalis intoxication (Sampson and Anderson, 1932) (4) bromides, preferably ½ to 1 gm (7½ to 15 gr) of triple bromides (of sodium, potassium and ammonium) in solution in a few ounces (60 to 90 cc) of water two or three times a day (5) digitalis, as a pill of the powdered leaf standard strength (see Chapter 30) 0 06 gm (1 gr) three times a day for a week, and (6) papaverine hydrochloride 1½ gr four times a day In various cases each one of these remedies has proved effective but in many cases no one of them controls the premature beats. Bromides should be used for short periods of time only because of the hazard of toxic effects. Strychnine given with quinidine has also been recommended when quinidine alone is not effective (Carter and Trust, 1935) The very absence of specific therapy however has flooded the market with remedies of reputed but doubtful value.

Differential diagnosis. Premature beats must be differentiated from sinus arrhythmia and heart block. This can in most cases be done easily without an electrocardiogram, and in doubtful cases easily with such a record. The usual disappearance of premature beats caused by increasing the heart rate by exercise helps to differentiate a gross arrhythmia due to many premature beats from the absolute arrhythmia of atrial fibrillation which increases on exercise. The clear prematurity of a cardiac contraction followed by a pause longer than the usual interval between two normal heartbeats in an otherwise regular rhythm establishes the diagnosis of a premature beat. Exceptions, like interpolated premature beats needing graphic records have been discussed above.

Premature beats are a sign of one type of "irritable heart" but their occurrence is not to be confused with the so-called "irritable heart of soldiers," which in the vast majority of cases has proved to be neurocirculatory asthenia, nor is it to be classed as cardiac neurosis, although such a condition may be superimposed.

And, finally angina pectoris is not to be diagnosed when all that a patient complains of is a sharp stabbing pain in the precordium caused by a premature beat.

PAROXYSMAL TACHYCARDIA

Paroxysmal tachycardia is a common disorder of cardiac rhythm closely related to premature beats, first mentioned by the ancients, in particular Galen, but not clearly recognized as a characteristic disorder until Bristowe described it in 1888 It was given its name the following year by Bouveret (1889)

Bristowe, J S. "On Recurrent Palpitations of Extreme Rapidity in Persons Otherwise Apparently Healthy *Brain*, 1888 X, 164

This paper by Bristowe, clearly describing paroxysmal tachycardia as clinical entity for the first time, antedated by a year the report by Bouveret in which the term "paroxysmal tachycardia was first used. The following quotations are of interest

"The subject to which I wish to direct ttention is that of extremely rapid pulsation, occurring for the most part in intermittent paroxysms of variable duration, in hearts structurally and texturally sound, and in persons otherwise healthy

"That hearts may beat with the extreme rapidity with which I have found them to beat, is a fact which, I think, has been largely overlooked, and with which I, at any rate, had no practical acquaintance until within the last two or three years, and yet I feel sure, judging from my recent experience, that the condition which I am about to discuss is of frequent occurrence, and needs only to be looked for intelligently to be recognized in many persons who are regarded as merely nervous and liable to attacks of ordinary palpitation.

"So far as I know the literature of the subject was, until recently limited to the report in the 'British Medical Journal for the year 1866, of three well-marked cases, the first from the pen of the late Dr Cotton, and the others respectively by Dr. James Edmunds and the late Sir Thomas Watson. Of these cases I need only say that they almost accurately resembled the most striking and typical of the cases which are incorporated in this paper

"The first typical case of the disease which I ever fully recognized was one which I saw in consultation with Dr Wyman of Putney in the early part of 1885 The patient was a fairly healthy-looking young married lady who had evidently been liable for some years to attacks of palpitation, and was free from structural disease of the heart. The ttack in which I saw her came on suddenly without apparent cause, and after a week left her as suddenly as it had arisen. Her pulse varied between 180 and 192 in the minute. A few weeks later she had recurrence of palpitation, when the cardiac beats were counted at 46. What seemed to me at the time the most remarkable feature of her case was the apparent absence of distress. Had I not known that the patient's heart was beating with extraordinary rapidity it would

never have struck me, from watching her and conversing with her that there was *anything the matter with her*

Bristowe then proceeds to relate eight other cases with or without heart disease, and with or without arrhythmia attending the paroxysms of tachycardia. One case was evidently an instance of atrial fibrillation and yet this patient, a man 65 years old, was able to run 3 miles in 20 minutes. His first case, described above may of course, have had atrial flutter without block when the rate was 246 rather than the usual paroxysmal tachycardia (see Chapter 33) Among the conclusions of the paper the seventh is the most pertinent.

7 *As to the real nature of the disease which my paper is* intended to illustrate, I have little to say My belief is, as will doubtless have been gathered from all that precedes, that so far as the heart is concerned it is a purely functional disorder, that any actual cardiac disease which may be present in any case must be regarded as accidental, and that the slight hypertrophy and dilatation of the heart which may be found in patients who have suffered from the malady for years are (as I have already remarked) the consequence, and not the cause, of the palpitation.

Incidence. Paroxysmal tachycardia is very frequent but not so *universal* as are premature beats. Many individuals have short attacks of what they call "fluttering of the heart" for which they do not consult a physician, either because the attacks are not sufficiently bothersome or because they are so brief that it would be useless to summon one if they do seek medical advice, the paroxysms usually occur at times when they are not observed by the doctor. Many healthy friends of mine have complained of such attacks lasting usually but a few seconds or minutes and not sufficient in severity or duration to render them of more than passing interest, by special endeavor I have obtained electrocardiograms of some of these attacks when they have been repeated or have been longer than usual, but such success is rare because of the elusive nature of the paroxysms. These observations illustrate the frequency of the condition which is inaccurately represented in any statistical studies at present available, such as my own of a series of 132 cases, 89 (or two thirds) of whom showed no evidence of heart disease (White, 1926)

Ventricular paroxysmal tachycardia, though often serious, is a relatively uncommon type and is found only once to every six cases of atrial paroxysmal tachycardia in an electrocardiographic series of 103 cases of paroxysmal tachycardia at the Massachusetts General Hospital the origin of the abnormal rhythm was clearly in the atria in 80 and clearly in the ventricles *in 14*

Mechanism (abnormal physiology). Paroxysmal tachycardia appears to be due to a rapid, usually regular production of waves of excitation and contraction at some point in the atrial or ventricular muscle, generally outside the normal sinoatrial nodal pacemaker although rare instances of nomotopic or sinoatrial paroxysmal tachycardia have been reported. Electrocardiographic study shows that the separate excitation waves closely resemble those of atrial or ventricular premature beats. The exact mechanism of production of such a rapid succession of premature contractions is not clear theories have ascribed it to the rapid building up of a stimulus, as in the case of normal sino-

atrial tachycardia, which seems most likely or to constant circus movement of an excitation wave once started, or to some other unknown cause. Its main characteristics are its sudden onset and offset, its rapid rate (120 to 200 or rarely somewhat more usually 160 to 180) and its tendency to great regularity In the rare paroxysmal tachycardia of infancy the heart may attain an extraordinarily rapid rate of beating, even at 300 or more The fastest rate that I knew of at the time of the second edition of this book was in an infant whose heart rate was 312, the result of either atrial paroxysmal tachycardia with bundle branch block or ventricular paroxysmal tachycardia the infant died of bronchopneumonia erysipelas empyema, and meningitis but showed no abnormality of the heart at autopsy (Lyon, 1937) In 1937 Campbell reported three interesting cases of extremely rapid heart rates in infancy (300 274 and 266 respectively) two of whom had congestive heart failure during their paroxysms but recovered completely Later Hubbard published his important study of nine infants with paroxysmal tachycardia their rates were 270, 300 274 300 260 290 305 270, and 220 respectively (Hubbard, 1941) At the time of the third edition of this book (1944) I stated that I had seen electrocardiograms of a few very young infants with heart rates of 300 to 310, and had noted the remarkable case of a 10-day-old infant with a heart rate of 345 reported by Puglisi (1939) Since then even faster rates have been noted, for example, 365 per minute, unrecognized until just before death in the case of an infant (Silverman and Race, 1949)

(a) *Atrial paroxysmal tachycardia* Atrial paroxysmal tachycardia (Figure 156) is by far the most common and least important type of paroxysmal tachy

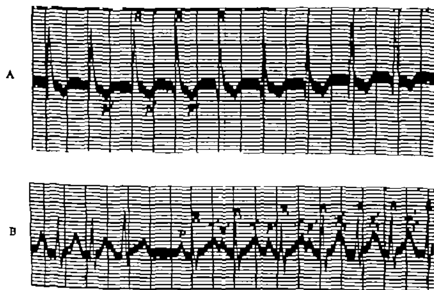


FIG. 156. Electrocardiograms (Lead 2) showing atrial paroxysmal tachycardia. (*A*) The usual mechanism, (*B*) an unusual variation with short runs of tachycardia and varying rate.

cardia, occurring about six times more often than the ventricular type. It is usually very regular at a rate of 160 to 180, but on rare occasions there may be a gradual onset, gradual offset, and some slight arrhythmia during its course. The abnormal contractions are usually represented in the electrocardiogram by inverted *P* waves in Leads 1 and 2, diphasic *P* waves in Lead 3, and inverted *P* waves in the precordial leads, but sometimes the *Ps* are upright with abnormal contour: the appearance of these ectopic atrial complexes may vary considerably with change in position of the heart due to forced breathing, the inverted *P* waves in Lead 2 during quiet breathing, for example, becoming diphasic or even upright on deep inspiration, resulting from the changed relationship of the position of the ectopic focus, and that of the heart. The abnormal *P* waves in atrial paroxysmal tachycardia are usually followed by normal ventricular responses at the same rate, but occasionally when the rate is very rapid there may be temporary atrioventricular or intraventricular block, so that 2 to 1 partial block or left or right bundle branch block may appear as a transient associated functional disorder of little or no clinical importance in itself. Rarely an atrial paroxysmal tachycardia may be interrupted by a ventricular premature beat.

(b) *Ventricular paroxysmal tachycardia.* Paroxysmal tachycardia of ventricular origin (Figure 157) is an important, frequent, and usually a serious disturbance of rhythm, similar in other characteristics to atrial paroxysmal tachycardia, except that it tends to be somewhat less regular in its rhythm. The arrhythmia, although obvious on electrocardiographic measurement, is evident clinically in only about half of the cases on close examination. The shape of the ventricular complex of the electrocardiogram is exactly like that of a ventricular premature beat, but in a few instances there is a variation in shape from beat to beat, in the most marked cases an alternate reversal of direction with slight alternation of time intervals (Figure 157C). When an alternating bidirectional character of the ventricular complexes of ventricular paroxysmal tachycardia is seen, the condition is invariably a serious one, usually terminal. The fundamental sinoatrial rhythm may or may not be disturbed by a paroxysm of ventricular tachycardia; usually it is at least quickened, even though it may remain independent: sometimes retrograde atrial responses follow each or every other abnormal ventricular beat in this variety of tachycardia. On occasion atrial fibrillation, and very rarely atrial paroxysmal tachycardia, may coexist with ventricular paroxysmal tachycardia. The differentiation of abnormal ventricular tachycardia into right ventricular and left ventricular types has been suggested, as in the case of ventricular premature beats (see Chapter 9 and the first part of the present chapter), but as yet the clinical value of such differentiation has not been shown.

(c) *Atrioventricular nodal paroxysmal tachycardia.* This is very rare. It has the relatively unimportant clinical significance of atrial paroxysmal tachycardia and a mechanism somewhat similar to that of ventricular paroxysmal tachycardia with regular retrograde atrial response, although in rare instances

the atrial contraction may precede the ventricular even when the impulse starts in the atrioventricular node

Electrocardiographic records are needed to differentiate clearly the different types of paroxysmal tachycardia, a phlebogram, if it happens to show the onset or offset of a paroxysm, gives a certain amount of information, but not clear enough proof.

A very interesting small group of cases of paroxysmal tachycardia, atrial mostly but sometimes ventricular consists of otherwise healthy young people who show by electrocardiogram, either constantly or temporarily short *P R* intervals. This syndrome will be discussed further in Chapter 34 but a clearer

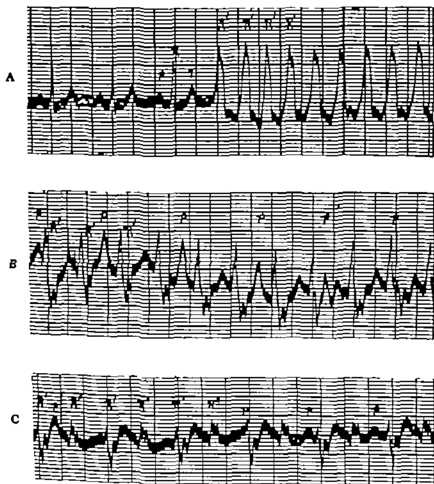


FIG. 157 Electrocardiograms (Lead 2) showing ventricular paroxysmal tachycardia (*A*) onset of the usual type, (*B*) with *P* waves clearly seen superimposed on the *QRS* and *T* waves and quite independent of them, and (*C*) with ventricular complexes alternating in direction (also called "bidirectional")

understanding of the mechanism of this syndrome might throw light on the mechanism of paroxysmal tachycardia itself

Etiology *Cause* Just how the abnormal mechanism of paroxysmal tachycardia is initiated is not known but certain causative factors are known. Conditions responsible for premature beats are likewise responsible for atrial paroxysmal tachycardia. Such factors are fatigue, sudden exertion, indigestion, tobacco, alcohol, digitalis poisoning, infection, and heart disease. As in the case of premature beats, heart disease is more often absent than present when there is atrial paroxysmal tachycardia, though here again a diseased heart is more often affected by paroxysmal tachycardia than is a normal heart. Often there is no known or discoverable cause for atrial paroxysmal tachycardia.

Ventricular paroxysmal tachycardia is found as a rule, but not always, in the presence of organic heart disease of serious type, and can be rapidly fatal if the electrocardiogram shows alternating direction of the complexes. Digitalis intoxication has been associated in a number of the fatal cases on record. In a few instances ventricular paroxysmal tachycardia occurs with little or no evidence of organic heart disease.

Sex Both sexes are probably affected about equally by paroxysmal tachycardia, of either atrial or ventricular type. In the series of my own of 132 cases noted above the females were preponderant in the ratio of 82 to 50, but in another electrocardiographic series of 80 cases of atrial paroxysmal tachycardia 42 were male and 38 were female, while of 13 cases of ventricular paroxysmal tachycardia proved electrocardiographically 8 were male and 5 were female.

Age Atrial paroxysmal tachycardia is common after childhood but rare in infants and young children. Ventricular paroxysmal tachycardia, rare at any age, is commonest in the serious heart disease of later life.

Family Incidence It is not uncommon for paroxysmal tachycardia to occur in several members of the same family

Pathology There is no pathologic condition in the heart characteristically found with paroxysmal tachycardia most cases of this disturbance of rhythm have apparently perfectly normal hearts. There are, however certain changes which favor paroxysmal tachycardia. Mitral stenosis is not infrequently accompanied by atrial paroxysmal tachycardia before the onset of permanent atrial fibrillation, but paroxysmal atrial fibrillation which also occurs in mitral stenosis must be differentiated from atrial paroxysmal tachycardia. The heart in thyrotoxicosis may be affected by either atrial paroxysmal tachycardia or paroxysmal atrial fibrillation, but more commonly by the latter And finally cardiac infarction is likely to be found responsible in the more serious cases of ventricular paroxysmal tachycardia.

Symptoms. Usually the person affected is conscious of the disturbance of rhythm, but in rare cases a paroxysm, long or short, may pass unnoticed except by the observer this happens in insensitive persons or in individuals who are too ill to appreciate this complication. The general complaint is of a regular rapid palpitation or of a disagreeable sensation of fluttering in the

chest in the region of the heart. The sensation may be widely referred over the body so that the vessels seem to pound in head and arms, abdomen and legs. A fullness in the neck is often complained of due to the transmission of the pulsation to the jugular veins. There may or may not be associated dyspnea and heartache, due in part, and in all probability chiefly to nervousness and fear in sensitive persons, and representing a kind of neurocirculatory asthenia, but dyspnea may also be due to cardiac fatigue in persons with hearts already weakened or overburdened, or occur after very long paroxysms lasting for days. Angina pectoris has sometimes been noted during the paroxysms in persons with coronary heart disease to start with giving rise to a *status anginosus* until the paroxysm subsides, and symptoms of congestive failure with engorgement of liver and lungs are occasionally produced by long paroxysms of tachycardia in patients with heart disease and rarely in persons without heart disease. With an extremely rapid rate in paroxysmal tachycardia the brain may receive little blood, and faintness, dizziness, and even syncope may ensue. If the pulse is faint or absent and unconsciousness and convulsions result from the extreme tachycardia, the condition may simulate the Morgagni-Adams-Stokes syndrome of high-grade heart block. An occasional symptom during or following paroxysmal tachycardia is increased frequency or increased amount of urination, doubtless a nervous reflex in large part.

Signs. The pathognomonic evidence of paroxysmal tachycardia is electrocardiographic (Figures 156 and 157) but any regular rapid rate of 120 to 200 per minute observed clinically to start abruptly and to stop abruptly and lasting usually a few minutes (with a range from a few seconds to several days) may be reasonably diagnosed as paroxysmal tachycardia without the need of graphic records. A striking feature of paroxysmal tachycardia is the uniformity of rate, as compared with ordinary sinoatrial tachycardia which varies in rate under various conditions, such as exercise, change of position, carotid pressure, deep breathing, and digitalis therapy A variation of a few beats per minute may however occur from time to time even in paroxysmal tachycardia, especially of the ventricular type and especially under the influence of quinidine.

Aside from the tachycardia there is usually no other sign. There may or may not be evidence of chronic heart disease and enlargement. Except when the heart is exhausted or diseased it is usually found by roentgen ray examination during a paroxysm to be decreased slightly or moderately in size below the normal, this is due to the fact that the rapid rate prevents full normal diastolic dilatation. Sometimes, even in the case of normal hearts, prolonged paroxysmal tachycardia may cause cardiac dilatation which is evident by roentgen ray The blood pressure is usually normal or somewhat decreased during a paroxysm, and the pulse small, due to the rapid rate. At times during a very rapid heart rate or after a long paroxysm, alternation of the pulse occurs, due doubtless to myocardial fatigue (Figure 33 page 162) pulsus alternans is not then the serious sign that it is with slower pulse rates the faster the heart rate, the less important the pulsus alternans. It is probable

that a healthy heart beating at a rate of nearly 300 per minute should normally show alternation of the pulse. The occasional development of intraventricular block at very rapid heart rates is likewise a more or less normal physiologic condition.

Signs of congestive failure may be found to begin or to increase in cases of heart disease during paroxysms of tachycardia. Very rarely a long paroxysm at a very fast rate may give rise to signs of failure even in the absence of heart disease this is especially true of the extreme tachycardias in infants, whose hearts and livers may become very large, shrinking rapidly when the attacks cease (Hubbard, 1941)

Electrocardiographic study is helpful during a paroxysm of tachycardia, particularly in differentiating the atrial type from the ventricular and in excluding atrial flutter Following a prolonged or very severe paroxysm of tachycardia the *T* waves of the electrocardiogram may become inverted even for some days and even in the absence of heart disease, due evidently to myocardial fatigue (Campbell, 1942)

Course and prognosis. Atrial paroxysmal tachycardia is usually unimportant. It is a transient disturbance, as a rule lasting but a few seconds or a few minutes and only rarely more than a few hours, sometimes occurring but once and sometimes repeatedly over a short space of time (a few days or weeks) It tends to recur off and on through life, but often at long intervals (years, for example) It generally neither shortens life nor limits activity but in some cases it necessitates rest during the paroxysms, and if the paroxysms are long or numerous there may be much crippling in a few cases complete invalidism may result. Heart failure and death are very rarely induced by paroxysmal tachycardia in a patient with heart disease, except in the case of atrial paroxysmal tachycardia complicating marked mitral stenosis or other pathologic condition where the cardiac reserve is low and failure easily induced, and in the case of ventricular paroxysmal tachycardia, which may be itself a terminal condition rather than a cause of death.

Like premature beats, paroxysmal tachycardia of atrial origin cannot be considered to be a diagnostic or prognostic sign of any importance. Diagnosis and prognosis must be based on other findings. Paroxysmal tachycardia of ventricular origin, on the other hand, must be considered serious until proved unimportant.

Complications. Only rarely is paroxysmal tachycardia attended by complications. The most important ones are (1) congestive heart failure in the presence of pre-existing heart disease and even without previous heart disease, especially if as in infants, the heart rate is excessively fast (300 more or less, per minute) (2) myocardial infarction in the presence of a high degree of coronary artery narrowing and due to the abrupt drop in effective coronary blood flow (3) the temporary status anginosus in coronary heart disease without actual infarction, (4) syncope which may be either a nervous reaction, the result of marked decrease in cerebral blood flow during the paroxysm, or due to a transient total cardiac standstill at the end of the paroxysm and before

the resumption of normal rhythm and (5) death from evolution of ventricular tachycardia into ventricular fibrillation.

Treatment. Usually no treatment of atrial paroxysmal tachycardia is needed if the attacks are brief and rare, that is, not more than ten or fifteen minutes long or oftener than once a month. If the paroxysms are long or frequent, however or even if they are short and infrequent but disagreeable, an attempt should be made to abolish them.

The treatment consists of therapy directed to stop the individual attack, and of therapy to prevent a recurrence of paroxysms.

(a) *Therapy of an attack of atrial paroxysmal tachycardia* should be as simple as possible and not include the administration of a great variety of unreliable remedies to which recourse is frequently had.

The following procedure has been found in the hands of experienced observers to be a good one to adopt. In the first place, it is usually wiser for the patient to remain quiet during the paroxysm, seated or recumbent, than to continue full or even partial activity although it is possible and sometimes necessary to complete a task or effort in progress at the time of the onset of the paroxysm. Usually the paroxysms are shorter during rest than during exercise, but occasionally the reverse is true, and if so, exercise should be prescribed, especially calisthenic motions of arm stretching or body bending, which may cause an abrupt cessation of the attack. Even in the resting position certain postures are sometimes uniformly or frequently effective in stopping paroxysms, for example, leaning forward in a chair with the head low or lying with the head lower than the rest of the body

If the paroxysm does not stop quickly after the patient has assumed the most satisfactory position, it is always worthwhile to try the effect of stimulation by firm carotid sinus pressure with the tips of two or three fingers for from five to thirty seconds high on the right side of the neck over the fullest carotid pulsation. If pressure on the right side is ineffective, the same procedure may be tried on the left side or moderately firm pressure with the finger tips may be exerted on either eyeball with the eye closed (oculocardiac reflex method) In about 10 per cent of all cases the reflex vagal effect of these pressure methods or of position changes are effective and the paroxysms stop abruptly and dramatically usually with great relief to the patient. Since these procedures are easy and, with rare exceptions, safe they are always to be recommended. Right carotid sinus pressure should be tried before the left and before ocular pressure, since it is more likely to be effective and since pressure on the neck is less disagreeable than that on the eyeballs. In very rare instances, carotid sinus pressure has been followed by cerebral vascular accidents, such as thrombosis, but I myself have never encountered such sequelae. Various other mechanical and reflex measures have been utilized in individual cases with occasional success, such as the induction of vomiting, firm abdominal pressure, application of an ice bag over the precordium, drawing out the tongue, forced respiration, and the Valsalva or Müller experiments (the former consisting of an attempt to expire forcibly with the glottis closed after

a deep inspiration, and the latter being an attempt to inspire forcibly with the glottis closed after a deep expiration) but these measures are not to be routinely recommended. Often the paroxysm ceases spontaneously and the particular measure being tried at the time may unjustly be credited with the cure.

Drug therapy of a paroxysm is often unreliable. The best all-around drug to try first is quinidine which may be employed if a paroxysm is long (more than an hour) distressing, or exhausting. Quinidine sulfate in tablet or powder form may be given by mouth (0 4 gm, or 6 gr every two hours for five doses under observation) this oral therapy has proved to be effective in cutting short the paroxysms in frequent cases in my experience and in that of others, but it cannot always be relied upon. In patients severely ill with ventricular (and in fact also atrial) paroxysmal tachycardia who have failed to respond to quinidine by mouth or who are too nauseated to take it, a convenient and effective method of treatment is the subcutaneous injection of 1 gm (7 gr) of quinidine lactate or hydrochloride (injectable) every 2 hours until the paroxysm ends or toxic symptoms of cinchonism appear Intravenous injection of 0 2 to 0 4 gm of quinidine lactate or sulfate directly and repeated every four hours as needed or in the form of a drip (3 3 gm or 50 gr dissolved in 500 cc normal saline or in 5 per cent glucose solution) administered until there is an effect has also been recommended occasionally striking benefit has been reported from this measure, but it is simpler safer and about as effective to give the drug by mouth or to use quinidine salts intramuscularly

Another drug that has been used to control paroxysmal tachycardia, especially by Starr and his associates (1933) is Mecholyl (acetyl-B-methylcholine chloride) which acts through its stimulation of the parasympathetic nerves (including the vagus) the Mecholyl was successful in from one half to twelve minutes in abolishing twenty-four attacks of paroxysmal tachycardia, ventricular or atrial, in nine patients of Starr s when injected subcutaneously in the dosage of 20 to 30 mg· it may however have untoward effects, consisting of the production of vomiting, dyspnea, asthma (stopped by atropine) pain, marked fall of blood pressure, and heart block. Atropine sulfate (1 mg or 1/60 gr in solution) should be at hand to inject immediately in case of toxic symptoms. Recently Mecholyl in larger dosage, 200 to 300 mg, has been found to be effective when given intranasally (Nathanson and Tober 1948)

More recently revived as drug therapy to induce vigorous central vagal stimulation by means of marked nausea is the administration of syrup of ipecac by mouth, 8 to 16 cc (2 to 4 drachms) at a dose, repeating it as needed to build up a vagal stimulation marked enough to stop the paroxysm of tachycardia or at least to induce vomiting, this measure is usually effective and not dangerous, but it is disagreeable and to be reserved for the most severe cases.

If a patient is in much distress and the paroxysm continues despite the measures described above, various other drugs may be tried. Bromides may be administered, 1 gm (15 gr) of the triple bromides every four hours for a few doses, as needed or rarely morphine 0 01 to 0 015 gm (1/6 to 1/4 gr) intra-

venously or subcutaneously: it is, however, very important to avoid using morphine, except in the rarest cases of severe prolonged pain, pulmonary edema, or shock or obstinate ventricular tachycardia, because of the very real possibility of establishing morphinism in the treatment of this disorder which is so often recurrent. Also bromides should be used for only short periods of time because of the hazard of toxic effects. In a few cases digitalis intravenously (two or three doses of 0.2 to 0.4 mg of digitoxin or of 0.1 to 0.5 gm of Digifolin, Digalen, or similar preparation for intravenous administration in 10 per cent solution, at intervals of four hours) or strophanthin intravenously 0.5 to 0.25 mg or (1/120 to 1/240 gr) once has been followed by a rapid cessation of a paroxysm of tachycardia, but often this treatment is ineffective, it should be tried only if other measures in the control of an obstinate attack have failed or if there are symptoms and signs of congestive failure. In infants with prolonged paroxysmal tachycardia at excessive rates Hubbard found that digitalis (Digifolin) in the dosage of 0.1 to 0.3 gm daily for one or two days was usually very effective and should be used at once in preference to any other treatment (Hubbard, 1941).

Another therapeutic measure which has been tried and recommended in cases of intractable paroxysmal tachycardia is the injection of novocaine (procaine) and of alcohol in the stellate ganglion, left or right (Coleman and Bennett, 1938; Leibovici, et al., 1939)—this procedure needs further testing before adoption, since it is still only in the experimental stage. Somewhat related has been the successful control of disturbing paroxysmal tachycardia occurring during cyclopropane anesthesia by the intravenous injection of procaine (0.1 per cent solution) (Kraft, 1947). Finally, magnesium sulfate in 10 per cent solution by slow intravenous injection (2 gm in 5 minutes) has been recommended.

(b) *Therapy of an attack of ventricular paroxysmal tachycardia.* A paroxysm of ectopic ventricular tachycardia is, as a rule, much more serious than a paroxysm of ectopic atrial tachycardia and, therefore, demands almost invariably emergency treatment. This consists of the use of quinidine or of procaine amide (Pronestyl). Quinidine may be given in the form of the sulfate by mouth, dosage of 0.4 gm (6 gr) to be repeated in one hour and again in another hour if the attack is still in progress unless the situation is very urgent, under which conditions the drug should be given intramuscularly in the form of the lactate, gluconate, or hydrochloride (injectable). Ampoules of solutions of these salts have been prepared for intramuscular use: 0.4 to 0.6 gm (6 to 9 gr) should be given and repeated at two hour intervals for several doses if necessary. Although intravenous medication has been used it is less desirable because of its toxic effects. Sedatives and even narcotics may be needed also, especially if the ventricular tachycardia induces severe dyspnea with pulmonary edema or status anginosus.

Recently procaine amide (Pronestyl hydrochloride) has been introduced both in the treatment and prevention of paroxysms of ventricular tachycardia. It is the most effective therapy yet found and is given in the dosage of 0.5 to

1.0 gm orally or intravenously the latter in 5 to 10 cc solution. It can be repeated at two-hour intervals as needed in direct therapy and every three to six hours orally as a prophylactic.

(c) *The prevention of paroxysms of tachycardia* is just as uncertain as is the treatment of an individual attack. In the first place, possible factors responsible for the occurrence of the paroxysms should be sought and eliminated; such factors may be fatigue, overuse of tobacco, tea, or coffee, constipation, indigestion, overeating, overexertion, focal infection, and heart failure. In the second place, there are certain positive measures which are sometimes effective. Quinidine sulfate in daily rations, constantly or at intervals (0.2 gm, or 3 gr in tablet or powder form three or four times a day) is frequently beneficial, reducing or abolishing the paroxysms in about half the cases. In rare individuals, when the quinidine is ineffective, digitalization may work well, at least it is worth trying in obstinate cases in the dose of 0.06 gm (1 gr) of the powdered leaf (of the new international and U.S.P. standard strength—see Chapter 29) in pill form three times a day for a week for an adult of average size then, if effective, the digitalis may be continued in daily rations of 0.06 gm (1 gr) for as long as necessary. It is to be remembered that toxic doses of digitalis may themselves cause paroxysmal tachycardia, especially of ventricular type. Potassium salts have also been recommended for obstinate tachycardia, as in the case of premature beats. Stempien and Katz (1942) for example, have advised giving 1 or 2 gm of potassium chloride or acetate every two to four hours to supplement or reinforce the action of quinidine. Bromide therapy 1 gm (15 gr) of the triple bromides once or twice a day may be useful in relieving the discomfort and worry caused by the paroxysms, even if not in reducing the number and duration of the paroxysms themselves. Finally thoracic sympathectomy has been introduced to prevent or to decrease the incidence of obstinately recurrent paroxysmal tachycardia but with as yet inconclusive results.

Reassurance is always an important part of the treatment and may itself suffice to get rid of the major part of the patient's unfavorable reaction to the attacks. Moreover daily exercise in the open air may have a salutary influence on an irritable heart.

Differential diagnosis. Paroxysmal tachycardia must be differentiated from extreme sinoatrial tachycardia, atrial flutter and atrial fibrillation. Its steady rapid rate and sudden onset and offset distinguish it from sinoatrial tachycardia. Its short duration (seconds, minutes, or hours rather than days, weeks, months, or years) the slower atrial rate (100 to 200 rather than 200 to 400) and the failure of atrioventricular block to be an almost constantly associated condition, distinguish it from atrial flutter. Its regularity of rhythm distinguishes it from atrial fibrillation. To differentiate atrial from ventricular paroxysmal tachycardia with certainty an electrocardiogram is necessary though clinically a slight arrhythmia favors the diagnosis of the ventricular type.

Finally the abruptness of the paroxysms of tachycardia may now and then result in confusion with heart attacks other than arrhythmias, especially

angina pectoris, coronary thrombosis, and acute dyspnea careful analysis should easily prevent such confusion, except perhaps in rare cases actually suffering from two different kinds of heart attacks occurring simultaneously (in which case the tachycardia may induce anginal pain or acute heart failure) or occurring alternately

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CHAPTER 33

ATRIAL FIBRILLATION AND FLUTTER VENTRICULAR FIBRILLATION QUINIDINE THERAPY

Although it is quite possible that atrial fibrillation and flutter are, as manifestations of abnormal physiology simply more advanced stages of the same process that gives rise to atrial paroxysmal tachycardia, they are so different clinically from that disorder of rhythm that they demand an entirely separate chapter

Moreover although atrial fibrillation and atrial flutter are themselves very closely related in mechanism, undoubtedly representing simply different stages or gradations of the same underlying process or disturbance of cardiac rhythm, they do not, however have the same clinical characteristics and they differ somewhat in treatment. They will, therefore be considered separately in this chapter Atrial fibrillation though apparently a more complicated mechanism than atrial flutter is far more common and clinically more important and so will be considered first.

ATRIAL FIBRILLATION

Introduction. Atrial fibrillation is one of the commonest, most interesting, and most important disorders of cardiac rhythm it is fundamentally a disturbance of atrial origin and attended usually by absolute irregularity of ventricular action. Its clinical existence, suspected by Hering in 1903 and by Cushny and Edmunds in 1906, was proved in 1909 by Rothberger and Winterberg, and by Lewis independently

Rothberger C. J and Winterberg, H. "Vorhofflimmern und Arhythmia perpetua. *Wien. klin. Wchnschr* June 17 1909 XXII, 839

Rothberger and Winterberg were the first to publish satisfactory evidence that atrial fibrillation occurs in human patients; their publication antedated by only a few months the independent demonstration by Lewis that atrial fibrillation is a common clinical condition. I have selected and translated few sentences from this work of Rothberger and Winterberg.

Although the pulsus irregularis perpetuus has been known to clinicians for a long time, it has only in recent years been described, by Hering (1903) as a special form of cardiac arrhythmia, characterized by particular features

"The normal venous pulse curve shows with each heart beat three characteristic upstrokes, the first of which precedes the apex impulse, that is, the pulse in the great arteries, and represents atrial systole.

In arrhythmia perpetua this wave, which gives us evidence of activity of the right atrium is entirely missing, and the phlebogram shows the characteristics of the so-called positive or ventricular venous pulse.

"There has long been known in animal experimentation a very irregular heart rhythm, namely atrial fibrillation (Flimmern der Vorhofe) which is identical in all details with the signs of arrhythmia perpetua.

"Atrial fibrillation is accompanied by absolutely irregular ventricular action, transmitted to the pulse: thus arrhythmia is of exactly the same character as that which we find in arrhythmia perpetua.

In atrial fibrillation more or less delicate fibrillary movements occur which are of no significance for the movement of blood as a result in the phlebogram the preventricular wave is missing and a positive venous pulse develops.

The authors then describe electrocardiograms from experimental animals and from patients, pointing to the three points of similarity between the records from animals with known atrial fibrillation and the records from patients with absolute arrhythmia (arrhythmia perpetua) These three points of resemblance are (1) absolute ventricular arrhythmia, (2) absence of *P* waves, and (3) presence of irregular oscillations of the galvanometer string due to the fibrillary waves themselves.

Lewis, Thomas. "Auricular Fibrillation a Common Clinical Condition. *Brit. M J* November 27 1909 II, 1528

Lewis also published convincing evidence of the frequent clinical occurrence of atrial fibrillation.

It is well known that in the late stages of mitral stenosis, and in cases of general cardio-vascular degeneration, the pulse is frequently continuously and extremely irregular The type of irregularity is remarkable in that in radial and cardiographic curves it defies analysis. The nature of the arterial curves has given rise to the term pulsus irregularis perpetuus, and it has been supposed that the rhythm of the heart producing it has its origin in the node of T wara (hence the term 'nodal rhythm') The condition is extremely common.

Facts are now at my disposal permitting of two conclusions.

I. That a rhythm arising in the neighbourhood of the node gives rise to a totally different clinical picture. This conclusion is based upon a detailed examination (polygraphic and electrocardiographic) of a case of paroxysmal tachycardia, in which it can be demonstrated that auricle and ventricle contract together This rhythm is a rare clinical phenomenon.

II That the irregular pulse of mitral stenosis, etc., already referred to, is due to fibrillation of the auricle.

"The second conclusion is based upon the following evidence.

1 The clinical irregularity presented by arterial and heart apex curves is unique. The rhythm is entirely disorderly and the sizes of the beats do not correspond to the pauses which precede them. Fibrillation of the auricle results in a

similar action of the ventricle and its action under these circumstances is unique experimentally

"2. Electrocardiograms taken from patients exhibiting the irregularity show a number of irregular waves, apart from the ventricular curve; they are more clearly defined in diastole. They are found in no other disorder of the heart's action. They disappear when, in a paroxysmal case, the irregularity vanishes, and are therefore due to a temporary and disorderly action of some part of the heart wall. Cardiographic curves give no evidence of such a disordered action in the ventricle. Fibrillation of the auricle yields curves which are identical in every respect, and no such curves have been obtained by any other experimental means. Further the waves on the experimental electrocardiograms can be shown to correspond to the fibrillary movements in the auricle, by means of synchronous tracings.

"3 The venous curve in the clinical irregularity is of the ventricular type; all the prominent waves occur during ventricular systole, and there is no wave corresponding to a normal auricular contraction. The same statement applies to the venous curves in fibrillation of the auricle. The clinical and experimental curves are of the same nature.

Incidence. Atrial fibrillation is common, ranking probably third in frequency as a disturbance of rhythm, premature beats and atrial paroxysmal tachycardia ranking first and second. Most statistics, especially hospital figures, indicate that atrial fibrillation is more common than paroxysmal tachycardia, but this is almost certainly due to the fact that atrial fibrillation is a striking disorder usually permanent and easily recorded graphically while paroxysmal tachycardia is a transient disorder often overlooked or scarcely heeded, and difficult to record graphically because of its short duration. Atrial fibrillation, even of paroxysmal type, rarely escapes notice and almost without exception comes eventually under medical scrutiny In a group of 3 000 patients with cardiac symptoms or signs analyzed in New England (White and Jones, 1928) 376, or 12.5 per cent, were found to have atrial fibrillation, 309 (82.2 per cent) of which were permanent and 67 (17.8 per cent) paroxysmal in type.

Mechanism (abnormal physiology). Absolute irregularity of the action of the heart, termed in the past "delirium cordis" and absolute or perpetual arrhythmia, was attributed at first to a variety of different mechanisms, among them atrial paralysis with idioventricular rhythm, atrioventricular nodal rhythm controlling both atria and ventricles, and the conflicting activity of multiple incoordinated abnormal atrial pacemakers. Then for many years it was widely believed that the condition is due to the establishment of a wave of excitation and contraction constantly circulating at a more or less irregular but very rapid rate about a more or less irregular and variable ring of muscle in the atria, chiefly about the great veins, giving off stimuli to the rest of the atrial muscle and to the ventricles, the ventricles responding as rapidly as they can but at an irregular rate (Lewis, 1921) This conception was based on fundamental observations of the circus movement of muscular contraction waves in experimental animals (Mayer 1908 Garrey 1912–1914 Mines, 1914) It was shown that a contraction wave may continue to circulate around

a band of muscle, if such a band is long enough to allow the point of origin of the wave to recover from its refractory (nonresponsive) stage by the time the circulating wave reaches it again and that such a circus wave can apparently be established in the dog's atrium by a rapid series of faradic stimulations. The circus wave has been thought to be the underlying mechanism of both atrial flutter its simplest manifestation, and atrial fibrillation, its more complicated form. Recently however this theory of the "circus" movement has been challenged and another mechanism, namely that of excessively rapid atrial discharge of stimuli from one atrial focus, proposed in its place (Scherf, et al. 1948 Prinzmetal, et al., 1949) The "flutter" waves have been clearly visualized by the use of slow motion pictures and have been seen to travel in all directions from an irritated focus and not in the form of a circus, also it has not been stopped by a burn placed across a "circus" path (Prinzmetal, et al. 1949) Thus, this new explanation of flutter and fibrillation of the atria relates them closely to the mechanism of ordinary paroxysmal tachycardia, the difference being simply that of rate. However several difficulties remain to be explained, including the rarity of atrial rates between those of flutter and of paroxysmal tachycardia, the electrocardiographic differences, and, finally the clinical dissimilarities. More studies of this problem are obviously needed.

The rate of initiation of the excitation and contraction wave in the atrial muscular tissue in atrial fibrillation is very rapid, averaging in man about 400 per minute and varying between 300 and 500 The speed is so great that areas of block or refractory points develop accounting for the irregularity of rate seen in the electrocardiogram, as regards both atrial and ventricular action Related to this same mechanism is that found in atrial flutter where the excitation occurs at a slower and much more regular rate (though not always absolutely regular) at 200 to 400 per minute, averaging 300. Transitional stages between fibrillation and flutter are common at atrial rates of about 350 and they have been variously called "impure flutter" "flutter-fibrillation," and "coarse fibrillation," the last term referring to the coarse atrial deflections seen in the electrocardiogram a halfway stage between the wide regular oscillations of flutter and the fine irregular movements of fibrillation (Figure 158) A new term "auricular tremulation" has been suggested for this intermediate stage (Pinchenzon, 1937) but it seems unnecessary to multiply designations for the mechanism responsible for both "atrial fibrillation and "atrial flutter"

The ventricular response to the very abnormal atrial mechanism in atrial fibrillation is almost invariably grossly irregular and rapid when first encountered, at about 130 to 150 per minute, before therapy has been instituted and in the absence of organic or functional heart block. Heart block, either permanent from disease or temporary from the functional effect of drugs, reduces the ventricular rate but does not control the ventricular arrhythmia unless the block is rendered complete

It is of interest to observe that in spite of the loss of sinoatrial control of

the heartbeat, outside influences can still affect the heart (ventricular) rate when there is atrial fibrillation, apparently through the action of the vagus and sympathetic nerves on the atrioventricular node and bundle thus excitement and exertion *will increase the heart rate*, and *changes in rate with respiration* are often seen, especially in sensitive, nervous persons with neurocirculatory asthenia. In rare instances the ventricular rate may be controlled by ventricular

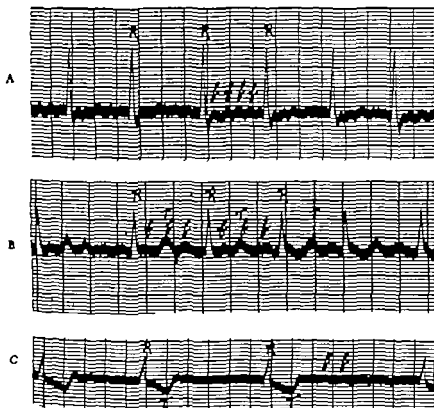


FIG. 158 Electrocardiograms (Lead 2) showing atrial fibrillation. (*A*) "Fine type with high rate of atrial action, (*B*) coarse type with slow rate of atrial action, (*C*) atrial fibrillation with considerable degree of atrioventricular block (ventricular rate below 60) and inverted *T* waves (digitalis effect)

pacemakers in spite of the presence of atrial fibrillation. This happens in three conditions (1) complete heart block, (2) ventricular paroxysmal tachycardia, and (3) ventricular escape or idioventricular rhythm superimposed on partial block, when for some reason, as from digitalis stimulation, the atrioventricular node becomes sufficiently irritable to control the ventricular action at regular rates of moderate speed, usually about 60 to 90 per minute. "Ectopic" contractions arising in the ventricle also often *interrupt the arrhythmia* induced by atrial fibrillation this is most strikingly seen when every beat of supraventricular origin is followed by a premature beat to produce the

so-called bigeminal or coupled pulse, characteristically found with digitalis intoxication. It is of interest to note that in such cases the ectopic or premature ventricular beats are always evenly spaced after the preceding beats of supraventricular origin even though the pairs occur irregularly The explanation of this regular interval between the first and second beats of the couples in the bigeminal rhythm of atrial fibrillation is not certain, but it is probably due to re-entry of the normal beat at some point of local block or prolonged refractory period, the muscle failing to respond at that point to the original stimulus but able finally to contract and to start a new heartbeat in adjacent muscle (which has recovered from its own refractory phase) when the original stimulus reaches it by a circuitous route.

The speed, length, and points of block (or refractory state) of the flutter wave in the atria determine its existence as flutter or as fibrillation. Certain factors, particularly two drugs, influence these conditions.

Digitalis tends to cause intra-atrial block by increasing the refractory period through its direct action on the atrial muscle, but its usual chief effect is to increase the rate and irregularity of the excitation wave and to shorten or hasten its course by decreasing the refractory period of the muscle through vagal action this vagal action overrules the direct effect on the muscle. In this way digitalis acts to convert atrial flutter into atrial fibrillation, and sometimes this is followed by a return of normal rhythm. Digitalis, while increasing the atrial rate, practically always slows the ventricular rate in atrial fibrillation by increasing the grade of atrioventricular block, except in rare cases when massive doses may cause a regular idioventricular rhythm or ventricular paroxysmal tachycardia.

Quinidine sulfate slows the excitation wave (more effectively than quinine) by increasing the refractory period of the atrial muscle at the same time that it increases its duration this increase in duration probably is necessary for the continuance of the atrial action which otherwise would always be quickly stopped (as it sometimes is) by the increase in the refractory period. The depressant and paralyzing action of quinidine on the vagus nerve acts to reenforce the direct effect of quinidine on the atrial muscle. The excitation wave takes a slower and more regular course under the effect of the quinidine. This drug has therefore a tendency to convert atrial fibrillation into atrial flutter It also tends to increase the ventricular rate when the atrial rate falls. If the increase in the refractory period of atrial muscle under quinidine therapy is so great that it overbalances the longer duration of the excitation wave, the latter may be unable to continue and the abnormal mechanism abruptly ceases. When at such a time the sinoatrial, or rarely the atrioventricular node resumes action a regular heartbeat results but if both of these nodes are themselves depressed by the drug, the heart may cease action altogether a probable explanation of death that has occurred in a few cases under quinidine treatment when embolism was not responsible.

Thus, the atrial rate may be increased in rate by digitalis from under 300 per minute to over 500 while the reverse is the effect from quinidine. E en

though the usual experimental data and theoretical considerations indicate that digitalis and quinidine may act in opposite ways on the refractory period of the atrial muscle and thereby cause opposed effects, clinical experience has shown that often it is worthwhile to digitalize before administering quinidine, partly because normal rhythm is more readily restored thereby and partly because the ventricular rate is kept from rising too high when the rate of the atrial contractions is reduced by the quinidine. It is also possible that fixed atrial flutter may be *prevented* by *preliminary* digitalization, although of that there is as yet no proof.

Finally it should be stated that atrial fibrillation is by no means a constant or "perpetual" condition as was at one time thought, it is frequently paroxysmal in nature, although, once established for a period of several weeks, it does tend to persist.

Etiology *Cause.* The cause of the establishment of the abnormal mechanism of atrial fibrillation is often obscure. In most cases there is an important grade or type of heart disease, or an important toxic or disease process of other nature, but sometimes there is no such cause, the individual seeming perfectly healthy without heart disease or poisoning of any sort. Thus the condition is fundamentally a functional disorder and not in itself to be classed as heart disease.

Atrial fibrillation is attended usually by little or no myocardial degeneration or inflammation, but nearly always an unusual degree of strain or nervous excitability exists. Mitral stenosis and thyrotoxic heart strain are the two cardiac conditions relatively most often associated with atrial fibrillation hypertension and coronary heart disease are only occasionally complicated by this arrhythmia. Aortic valve disease, congenital defects, syphilitic aortitis, and bacterial endocarditis are uncommonly associated with atrial fibrillation, probably because the atrial strain and nervous stimulation are less. The mystery of the rarity of atrial fibrillation in subacute bacterial endocarditis may be explained by the fact that this infection only infrequently attacks mitral valves that are badly stenosed and that it selects rather the aortic valve and slightly deformed mitral valves, from which defects there is little or no atrial strain. Atrial fibrillation is more common when the left atrium is under strain or enlarged, no matter what the cause of the enlargement, than when it is of normal size the commonest causes of such strain and enlargement are mitral valve deformity (especially stenosis) and failure of the left ventricle due to hypertension, myocardial infarction, or advanced aortic valve disease.

Once upon a time it was customary to label any individual over the age of fifty years who showed atrial fibrillation and nothing else wrong as an "arteriosclerotic" (meaning coronary) cardiac victim but now it is realized that such designation is unjustified it is perfectly true that cardiac arrhythmias, like gray hairs, are more common with increasing years and that a less adequate coronary circulation may be somewhat responsible, but, by and large, even in older persons, it is wiser in the absence of other evidence, to regard atrial fibrillation as a disorder of function rather than as a sign of heart disease.

Noncardiac etiologic factors responsible occasionally for atrial fibrillation, either in paroxysms or in established form, are poisoning by toxic agents of all sorts, such as excessive use of tobacco and alcohol especially in unaccustomed amounts on an occasional "spree," gas poisoning, food poisoning, and infectious diseases (like pneumonia) Sometimes violent exertion and excitement, trauma, and surgical operations (especially of the thorax) are responsible for the onset of paroxysmal or permanent atrial fibrillation, with little or no heart disease. In a group of 49 cases of atrial fibrillation without heart disease reported by Orgain, Wolff and White (1936) the exciting factors responsible for the onset of atrial fibrillation (paroxysmal or permanent) were apparently pneumonia, malarial chill, pelvic abscess, burns, surgical operation, ether alcohol, gallbladder colic, vomiting, exertion, and emotion (excitement and fear)

Finally there appears to be some sort of susceptibility or nervous hypersensitiveness that predisposes to this abnormal mechanism. Several members of one family may be affected, even in youth, without serious disease, and in fact in some cases without any evident disease at all.

In an analysis of 575 consecutive cases of atrial fibrillation reported by McEachern and Baker (1932) the chief etiologic relationships were as follows rheumatic heart disease 34 4 per cent, coronary disease and old age 31 1 per cent, hypertension 16 9 per cent, thyrotoxicosis 7.5 per cent, emphysema 5 0 per cent, syphilis 3 0 per cent, and miscellaneous 2.1 per cent. In the series of 376 cases of atrial fibrillation reported by White and Jones (1928) 346 patients had definite evidence of organic heart disease, while 30 (8 per cent) were apparently free from heart disease. Almost half 158 (45 6 per cent) of the organic group of 346 cases belonged to the rheumatic type, with or without complications. Seventy-four (21 4 per cent) of the cases had coronary heart disease without other complications 15 (4.3 per cent) had hypertension alone, while 92 others (26 6 per cent) had hypertension complicating other conditions and 14 (4 0 per cent) had thyrotoxicosis alone.

Sex The sexes are unequally affected by atrial fibrillation, paroxysmal and permanent. It was stated in the second edition of this book that about twice as many males as females show this arrhythmia, perhaps because men are generally subject to greater strain than are women a more recent review of 10 000 cases, which included 645 patients (6 45 per cent) with atrial fibrillation, electrocardiographed at the Massachusetts General Hospital from January 3 1939 to February 6, 1942, showed a ratio of 71 per cent males (455 cases) to 29 per cent females (190 cases)

Age Atrial fibrillation is very rare in infancy and early childhood, uncommon in adolescence, but increasingly more frequent in each decade of life as is generally true in the case of all other disorders of heart rhythm. Of the 575 cases of atrial fibrillation reported by McEachern and Baker (193) 0.5 per cent were under ten years of age, 4.2 per cent ten to twenty years old, 5 4 per cent twenty to thirty 15 0 per cent thirty to forty 20.2 per cent forty to fifty 26 1 per cent fifty to sixty 20.5 per cent sixty to seventy 7 8 per

cent seventy to eighty and 0.3 per cent eighty to ninety Despite the falling off in the figures of absolute incidence in the last three decades of life, atrial fibrillation actually continues to increase in frequency relative to the rapidly decreasing number of persons surviving to advanced age.

Pathology There is no pathologic change characteristic of atrial fibrillation. There may or may not be organic heart disease usually there is. There may or may not be myocardial abnormality other than hypertrophy usually there is not. Extensive heart disease, myocarditis, and myocardial degeneration may exist without atrial fibrillation. The atria are usually enlarged (dilated) in atrial fibrillation and their walls may show areas of degeneration and fibrosis which, however are neither uniform nor specific.

Symptoms. Atrial fibrillation especially if it is of permanent nature and properly treated, may exist without any symptoms. Usually however the patient is aware of the irregular heart action, which he describes variously as fluttering, irregular palpitation or pounding, skipping, or tumultuous action. This *consciousness of the abnormal heart action is particularly marked during* paroxysms of atrial fibrillation and at the time of the onset of permanent atrial fibrillation, before the ventricular rate has been controlled. At such times the distress, nervous irritation, and fear or worry may be so great that the patient feels, and may even be thought to be, far sicker than he is. He may be greatly distracted with the thought of impending death and a feeling that his heart must burst or stop after its vigorous leaping about. Even after full reassurance much discomfort usually persists, and, although the fear is gone, complete or partial invalidism may come with every paroxysm of atrial fibrillation, or may persist if the paroxysms occur frequently or if the arrhythmia becomes permanent. Gradually after the patient becomes accustomed to the recurrent paroxysms or to the constant arrhythmia, especially if the ventricular rate is controlled by treatment, the symptoms decrease and as a rule finally disappear entirely

Palpitation is the characteristic symptom of atrial fibrillation. Dyspnea and pain are much less common, but they may develop as a part of neurocirculatory asthenia if there is an associated marked psychic element (from fear and nervous exhaustion) dyspnea may set in if myocardial fatigue or pulmonary engorgement due to mitral stenosis develops as the result of the rapid irregular heart action, or the distress of an angina pectoris may appear due to extra work imposed by rapid heart action on a myocardium very badly supplied with blood. Other symptoms of the frequent complication of congestive failure are occasionally seen. The rarity of the association of atrial fibrillation with angina pectoris is an interesting problem, best explained by the limitation of activity that occurs with atrial fibrillation because of palpitation, dyspnea, fear or medical advice, there being no longer enough strain on the myocardium to exceed the reserve of the limited coronary circulation. When the heart action is very rapid in atrial fibrillation, there may be weakness, dizziness, and faintness, due in part at least to cerebral anemia. As in the case of paroxysmal tachycardia, syncope may rarely occur at the end of a paroxysm

of atrial fibrillation, due to failure of the normal pacemakers of the heart to resume action at once.

Signs. The characteristic sign of atrial fibrillation is absolute irregularity of the beating of the heart, whether the rate is rapid or slow Although this sign is not absolute proof of atrial fibrillation, there are very few exceptions (gross sinus arrhythmia, multiple premature beats, and atrial flutter with varying grades of heart block) Graphic records are useful in confirming the diagnosis of atrial fibrillation but they are usually unnecessary so far as this one particular finding is concerned a phlebogram will show atrial fibrillation, but an electrocardiogram is of more value, since it gives other additional information, for example, the effect of digitalis on the *T* waves (Figures 152, page 832, and 158C, page 897) and the state of the coronary circulation.

Often when the patient is first seen, before treatment is started, the heart action may be so rapid, irregular and weak that some beats fail to cause pulsation in the peripheral arteries as a result the apex rate is faster than the radial pulse rate and the difference is called the pulse deficit. When the ventricular rate slows as the result of rest and digitalis, the heart action becomes steadier stronger and more regular fewer beats or none fail to reach the wrist, until finally with a slow heart rate the pulse deficit entirely disappears, although, of course, the atrial fibrillation itself persists. The apex rate at first may be as high as 150 per minute and the radial pulse rate as low as 100, with a pulse deficit of 50 later after full digitalization, both apex and radial rates may be 75 with no pulse deficit at all the radial rate sometimes actually rises with improved strength of pulse as the heart rate slows. Generally at the onset the radial pulse rate is high as well as the apex rate and both drop with treatment (Figure 151 page 829) Although with training in palpating the pulse less deficit is found in cases of atrial fibrillation with rapid ventricular rate than before such training, nevertheless there often is an appreciable deficit at fast rates and to chart carefully several times a day the amount of pulse deficit along with the apex rate is one of the best ways to follow the effects of treatment. The observer usually a nurse, must be taught in such cases to record not only the radial pulse rate, but, what is much more important the apex heart rate also This procedure used to be neglected at times even in good hospital clinics or in private practice, and as a result there used to be considerable uncertainty about the course of the true heart rate of these cases, but in recent years this difficulty has been largely eliminated.

There may be no other signs of the abnormal atrial mechanism than the absolute irregularity of the heartbeat and the electrocardiographic evidence. Usually however there is some cardiac enlargement due to the presence of some sort of heart disease this may be great or little, or primarily of left ventricle, of right ventricle, or of the atria (especially of the left atrium in mitral stenosis) Murmurs may or may not be found, if present, they are due most commonly to mitral stenosis or to cardiac dilatation. There may be signs of congestive heart failure or of constrictive pericarditis.

The blood pressure may be normal low or high with atrial fibrillation

Often hyperpiesia is present and this important condition may be missed if the blood pressure is not measured Because of the difficulty of obtaining accurate figures of blood pressure in the presence of atrial fibrillation, especially with rapid ventricular rate, due to the greatly varying force of successive beats, sphygmomanometry was at one time largely abandoned in cases of atrial fibrillation or made very complicated by the use of special technic, such as taking the digital pressure and comparing it with the usual brachial standards or calculating the average brachial pressure by a fractional method. As a matter of fact, clinical experience in hundreds of cases has shown the feasibility and relative reliability of taking the blood pressure in the routine way in cases with atrial fibrillation. Although there is more or less variation in pressure of beats, a sufficiently accurate average can be quickly determined in a rough manner for both systolic and diastolic pressures. These pressure readings usually correspond quite closely to those of the same cases during normal heart rhythm, either before or after the atrial fibrillation. Moreover when the ventricular rate is slowed by digitalis the beats become much more uniform in force and may vary very little or not at all on blood pressure estimation there fore, if one is in doubt about the pressure in a difficult case sphygmomanometry can easily be repeated after the heart rate has been slowed or normal rhythm restored. Weak beats have a smaller pulse pressure with lower systolic and higher diastolic levels.

Roentgen ray study is not usually of much help although it is always essential to make such a study an integral part of a thorough examination of every patient with cardiac symptoms or signs. The ventricular arrhythmia is often evident fluoroscopically but it is less easily analyzed by roentgen ray than by auscultation or electrocardiography The abnormal atrial mechanism is generally indistinguishable by roentgen ray the atria appearing to partake only of the ventricular movement. Abnormalities of cardiac size and shape, if pronounced, are of course easily made out roentgenologically and may help, with the finding of atrial fibrillation, to establish such a diagnosis as mitral stenosis.

Electrocardiography is of the greatest assistance in confirming the diagnosis of atrial fibrillation, although this confirmation is often unnecessary Electrocardiography is still more useful in showing the presence or absence of associated abnormalities, like bundle branch block, and in following the effect of digitalis therapy on the *T* wave or of quinidine treatment on the atrial mechanism. The oscillations caused by the excitation wave in atrial fibrillation are usually best made out in Lead 2, but sometimes they are maximal in Lead 3 Precordial leads over the ventricles are usually disappointing, but if the exploring electrode is placed over the right atrium just to the right of the sternum in the position of the first of the six routine precordial leads, that is, in the fourth intercostal space, or better still in the third intercostal space just at the right of the sternum, the site of the so-called special atrial lead point (or over the left atrium esophageally) the *f* or fibrillation waves may be very evident.

Course and prognosis. Atrial fibrillation may be of trivial importance or it may be very serious. If it occurs in the form of transient paroxysms in a person

without heart disease it may be disagreeable but nothing more, recurring off and on at longer or shorter intervals or perhaps only once or twice without recurrence. Untreated paroxysms of atrial fibrillation usually last a few hours, with ordinary limits of a few minutes to several days, and very rarely extreme limits of a few weeks or months or even years (Fogel, 1943) Even if it occurs in permanent form atrial fibrillation may cause little or no disability if there is no important heart disease and if the heart rate is kept reasonably slow by constant digitalis therapy or controlled by organic heart block without drugs. Cases have been known with a history of paroxysmal or of permanent atrial fibrillation over periods of many years, even thirty or more. Paroxysms may occur only once or twice and be followed by long intervals of freedom for many years, or they may recur frequently at intervals of months or weeks and yet not cause disability or more than passing discomfort if the heart is strong.

In general, atrial fibrillation, like premature beats and paroxysmal tachycardia, is a functional disorder that in itself is a far less serious factor in crippling or in shortening life than is the underlying heart disease or other condition that may be present, provided that either the atrial fibrillation is transient or the ventricular rate is controlled by treatment. Now that quinidine therapy is successful in restoring normal rhythm in a good many cases of permanent atrial fibrillation, this type of atrial fibrillation can sometimes be transformed into that of paroxysmal nature with long intervals of months or even many years of freedom from any disturbing cardiac arrhythmia. Long lives of full activity may thus be carried on through the proper use of quinidine and digitalis in spite of the occasional occurrence of temporary disturbing paroxysms of atrial fibrillation or of the presence of permanent atrial fibrillation.

Complications. Unfortunately atrial fibrillation cannot always be regarded in so optimistic a way as that expressed above. Since it so often complicates very serious heart disease its occurrence may precipitate heart failure and even death, unless successful therapy is quickly instituted. It is always something of a burden even to a normal heart, though in such cases the cardiac reserve is sufficient to take care of the disorder The tachycardia rather than the arrhythmia is the serious factor and if that is reduced to a normal heart rate the circulation may be maintained in a satisfactory way in spite of the irregularity The fact, however that the circulation is more efficient with normal rhythm than with atrial fibrillation at the same heart rate makes it often worthwhile to attempt the restoration of normal rhythm, for there may come a time in an individual case when the more economic circulation maintained by normal rhythm means the difference between cardiac sufficiency and cardiac failure Although long-continued, uncontrolled atrial fibrillation alone may in rare cases cause a normal heart muscle to fail, the ordinary case of heart failure caused by atrial fibrillation is one showing extensive heart disease especially mitral stenosis. Proper treatment by digitalis and rest may prolong life for a number of years, probably sometimes for as many as ten or twelve but finally there comes a time, often at about forty-five to fifty years of age when

with advanced mitral stenosis the heart reserve can no longer be maintained and death comes in spite of the best treatment. The early recognition and early and persistent treatment of the atrial fibrillation which appears as a complication of heart disease is of great importance in prolonging life and reducing disability in cardiac cripples.

There is one condition thyrotoxicosis, in which atrial fibrillation, either in paroxysmal or permanent form is especially likely to be the earliest sign of cardiac strain. If the thyrotoxicosis is not corrected the atrial fibrillation may become established and even eventually cause heart failure and death, because the ventricular rate is difficult to control until the thyrotoxicosis itself is controlled. It is important always to consider the possible existence of thyrotoxicosis in any case of atrial fibrillation of unknown cause, that is, without sufficient pathologic change in the heart to account for it, particularly if it is difficult to control the ventricular rate with digitalis

An important complication of atrial fibrillation, besides heart failure, is embolism into cerebral, renal, splenic, or peripheral arteries, causing hemiplegia of varying degrees and duration and other evidences of infarction, the embolus coming from an intracardiac thrombus, usually in the left atrium. The stagnation of blood in the atria, when they have ceased coordinate contraction, favors the development of thrombi, especially in the appendages pieces of these thrombi may break off and be precipitated into the blood stream, more commonly in the systemic circulation, less commonly in the pulmonary circulation, the emboli getting loose either during the fibrillation or at the time of the return to normal rhythm which occurs either spontaneously or as the result of quinidine therapy The complication of embolism in atrial fibrillation is infrequent but often serious and sometimes fatal.

In very rare cases of mitral stenosis and atrial fibrillation there is formed free in the left atrial cavity a large spherical or "ball thrombus which, when it does occur partly occludes the atrioventricular ostium and may even temporarily obstruct it, to cause collapse of the patient; a unique case with ball thrombus in the right atrium has been discovered (Wright, et al., 1944)

Sudden death is rare in atrial fibrillation its cause is not known, although the onset of ventricular fibrillation has been suggested as responsible.

Treatment. The treatment of atrial fibrillation includes A, that of the condition itself and of its complications, and B therapy directed to prevent paroxysms of absolute arrhythmia or recurrence of the atrial fibrillation if once abolished.

A. **The direct therapy of atrial fibrillation** varies somewhat with the condition of the individual patient.

1 *Rest and digitalis* If there is congestive failure or very serious heart disease, quinidine should only very rarely be used, absolute rest should be enforced and full digitalization carried out as rapidly as necessary For an adult with atrial fibrillation who has not received digitalis or strophanthin and for whom emergency treatment is not needed, digitalis leaf in 0 1 gm (1½ gr) pills may be given at the rate of one pill three times a day for 4 or 5 days, or

0 06 gm (1 gr) three times a day for one week such a course to be followed by a ration of one pill daily of either dosage depending on the individual case, constantly thereafter so long as the fibrillation persists. This therapy should suffice to reduce the heart rate to normal by causing heart block, and to keep it normal this dosage is an average amount and may have to be decreased or increased in individual cases For emergency therapy 0.4 gm (6 gr) of standardized digitalis in solution (e g Digifolin) may be given intravenously to be repeated in four hours and again in the same or smaller amount in eight more hours if necessary or Cedilanid 4 cc (0 8 mg) may be given by vein to be repeated in four hours, or digitoxin 0 6 mg may be administered by mouth or vein and repeated in four hours or strophanthin (ouabain) 0.25 to 0 5 mg (1/240 to 1/120 gr) may be injected intravenously to be repeated in twelve hours if needed, these measures should be followed by a daily ration of one 0 1 gm (1½ gr) or 0 06 gm (1 gr) digitalis leaf pill. For further details of digitalis therapy see Chapter 30

2. *Quinidine therapy* A striking discovery concerned with the control of the functional atrial disturbance in fibrillation and flutter has been the therapeutic application of quinine and its isomer quinidine. The effective use of quinine in the control of "rebellious palpitation" was first mentioned by Senac in 1749 and rediscovered a century and a half later by a patient of Wenckebach (1914) another alkaloid of the cinchona bark, quinidine, an isomer of quinine, was found by Frey to be much more effective than quinine (1918) Although substitutes for commercial quinidine have been tried (see below) nothing more effective has been found as yet.

If the patient with atrial fibrillation has had no congestive failure or serious heart disease or history of embolism he should be considered a possible candidate for quinidine therapy At least two thirds of all such patients can be restored to normal rhythm by this treatment, and half of these, somewhat more than one third of the original total number can maintain normal rhythm for at least several months, sufficiently long to be considered definitely benefited by the therapy Some cases maintain normal rhythm for years, even for ten years or more in a few cases, with relief of symptoms and a return to normal active lives. One of my patients has maintained normal rhythm for twenty-five years, having been one of the very first cases of persistent atrial fibrillation to whom I gave quinidine soon after its introduction to this country Successful quinidine treatment has been an important accomplishment in medical progress

The percentages of successful restoration of normal rhythm in series of patients reported in the literature vary widely from 7 to 94 per cent, averaging about 60 per cent. This wide variation is due in part at least to selection of cases and in part to dosage and other factors. Two relatively recent reports give figures of 25 out of 34 cases (68 per cent) maintained for over three months in 16 (Laake, 1945) and 44 out of 50 cases (88 per cent) maintained in 20 for more than a month (McMillan and Welfare, 1947) The more normal the heart fundamentally the more likely is quinidine to act

successfully and safely Hence it is particularly indicated when the arrhythmia is simply a very annoying disorder of function. There are, however cases who are dangerously ill in whom the drug can be lifesaving, as for example (1) in restoring normal rhythm in a patient with congestive heart failure maintained by the tachycardia of his atrial fibrillation which is resistant to digitalis control, the heart rate being lower during normal rhythm in such cases than during atrial fibrillation, and (2) in reducing the likelihood of the deposition of further intra-atrial thrombi which might become emboli in patients with atrial fibrillation who have already suffered from embolism contrary to the classical rules of quinidine therapy (White and Blumgart, 1942)

The patient receiving quinidine in large dosage to restore normal rhythm should be under close observation, preferably in bed and where electrocardiographic observations can be made, so that the effect of the drug can be accurately followed and its toxic as well as its beneficial action noted. Since quinidine in large dosage is a poison, it must be used with care, and by the exercise of care accidents and fatalities that have been reported in rare cases in the past can largely be avoided. A good method of administration of quinidine that has been found effective is to give it by mouth in the form of the sulfate in tablets or powders of 0.2 gm (3 gr) each. A test dose of a single tablet or powder may first be given, to make sure that the individual is not unduly sensitive such sensitiveness is, however very rare. If no toxic symptoms (of cinchonism—see below) appear administration of the drug in large dosage can be begun. Of various schedules of dosage two are as follows (a) 0 4 gm (6 gr) that is, two tablets or powders, every two hours for five doses, for example, at 10 A.M. 12 M., and 2, 4 and 6 P M., making a total of 2.0 gm (30 gr) in the day continuing this regime for two or three days at a time if normal rhythm is not restored during the first day or on the following night, but stopping the drug on the appearance of toxic symptoms, normal rhythm, or obstinate atrial flutter (of more than three days duration) in a few cases 6 or 7 or 8 doses of 0 4 gm (6 gr) each at two hour intervals in a day have succeeded when the five doses have not (b) 0 4 gm (6 gr) every four hours day and night, except for the omission of one night dose during sleep, for a few days if necessary—the daily dose by this procedure will also equal 2.0 gm (30 gr) but this method is less reliable Sometimes smaller doses, down to one half the amount noted above, or larger doses, up to several times the above-mentioned amount (even 6 0 gm [100 gr] or more a day) have been given or recommended, but it is probable that the methods outlined here are as satisfactory as any and better than most. Massive doses of more than 4 gm (60 gr) of quinidine sulfate in a day are, in general, inadvisable and dangerous in the treatment of atrial fibrillation, but when life is in jeopardy after prolonged ventricular paroxysmal tachycardia, it is fair to take the risk of the larger doses (see Chapter 32)

In special emergencies or when the drug cannot be taken by mouth, quinidine can be given intramuscularly or intravenously preferably the former because of the danger of toxic effects from rapid administration by vein. It

can be given in the form of a solution of either the lactate, the gluconate, or the hydrochloride ("injectable") in the dosage of 0.2 to 0.5 gm (3 to 7½ gr) and repeated at two hour intervals as needed and as tolerated. On occasion, quinine dihydrochloride 0.5 gm (7½ gr) intramuscularly at two hour intervals has proved effective, but in general for the treatment of cardiac arrhythmias, quinine is inferior to quinidine.

So soon as toxic symptoms (cinchonism) of any important degree develop—marked tinnitus, deafness, urticaria, nausea, vomiting, diarrhea, intraventricular block (ascertained by electrocardiogram) and very rapid regular heart action—the drug should be discontinued. Observation of the patient should always be made for toxic drug effects before the administration of each new dose, and electrocardiograms should be taken several times during the day routinely at least after every other dose or even oftener An increase in ventricular rate is natural during quinidine therapy although it is not always encountered, when the atrial rate falls, atrioventricular conduction improves, so that the ventricular rate rises and atrial and ventricular rates tend to approach a common level therefore, even if a tachycardia develops, it need cause no concern if it does not exceed 130 or 140 if it rises higher the drug should be discontinued, for either the tachycardia may produce a very disagreeable palpitation or it may mean that there has developed a dangerous toxic heart rhythm such as ventricular paroxysmal tachycardia. An unusual toxic manifestation of the oral use of quinidine sulfate—high fever—has been reported (Sturnick, 1942)

If normal rhythm appears, the large doses of the drug should be reduced to daily rations for a shorter or longer interval, as desired, for example, one 0 2 gm (3 gr) tablet three or four times a day for a few weeks or the quinidine sulfate may at once be discontinued altogether If however the drug is continued every day for many months it tends eventually to lose its effect or it may cause annoying tinnitus, deafness, or looseness of the bowels, so that occasional periods are to be recommended in which the drug is withheld altogether for a few days or a few weeks if possible. Much judgment is necessary in dealing with an individual case, and experience with that case must control the therapy In fact the patients themselves often become expert in handling the situation and are then better able to arrange time and amount of doses of quinidine than are their physicians. For example, patients may find that they do not need the drug except at certain times during or just before some particular effort, against which they require special protection for their heart for a few hours or a few days. In such instances the quinidine should be taken by mouth about 1½ hours before the particular strain that tends to cause the atrial fibrillation. The effect of a dose of quinidine sulfate given by mouth reaches its height in 1 to 2 hours and ceases in 4 to 5 hours.

If persistent atrial flutter appears, it is best to stop the quinidine and to resort to digitalization to attempt to control this difficult disturbance of rhythm. Atrial flutter is a natural transitional stage in the change from atrial fibrillation

to normal rhythm, but it is usually brief and often too transient to be recorded electrocardiographically

Serious accidents can happen during quinidine therapy but they are very rare and, in carefully selected cases, very unlikely They include embolism due to pumping out by the heart of bits of intracardiac thrombus on restoration of normal atrial action. Embolism can, however occur with persistent atrial fibrillation alone and in fact does so then as often as upon the return of the heart to normal rhythm. Sudden death without embolism has also been noted in several cases during quinidine therapy and the cause has been variously explained by respiratory paralysis, cardiac paralysis, ventricular fibrillation or other mechanism. Cardiac standstill is the most likely explanation, being due to the paralysis of both pacemakers of the heart in the sinoatrial and atrioventricular nodes as the result of the toxic effect of the quinidine· when these nodes are depressed and the abnormal mechanism of atrial fibrillation is brought to an end by the drug there may be no available pacemaker to take up the function of exciting the heartbeat, death resulting. The finding of atrial standstill in two cases in which atrial fibrillation was abolished by quinidine has been noted by Wolff and White (1929) fortunately in these cases the atrioventricular node excited regular ventricular beats until the atria recovered their activity

Digitalis may or may not be used with the quinidine in the attempt to abolish atrial fibrillation. It seems to be helpful and is generally to be recommended though it is not always necessary It may be used in the dosage of 0.06 gm (1 gr) of digitalis leaf or 0 1 mg of digitoxin three or four times a day for five to seven days.

If normal rhythm is not restored by quinidine sulfate in the course of two or three days, the drug should be discontinued and full digitalization should then be established and maintained, if it has not already been accomplished. After a short interval of one to several weeks, a second course of quinidine sulfate, just like the first, may be administered if desired, and if that too is unsuccessful, even a third course may be given later after another interval, perhaps of a few months and with some variation of dosage. If digitalis is not used with the quinidine during an unsuccessful course, it may be tried with the next course. It is of interest and importance to note that occasionally a second or third course or a larger dosage of quinidine sulfate has proved successful after early attempts have failed.

In successful quinidine therapy normal rhythm is generally restored after a few doses on the first or second day of a course of the drug; infrequently atrial fibrillation may be banished by the single test dose or after the first regular dose of the course. Normal rhythm usually persists after its restoration for at least several weeks or months, and sometimes for years. If atrial fibrillation recurs it should be treated again in the same way as at first, but if it recurs often and normal rhythm lasts repeatedly for only a few hours, days, or weeks, it is best to abandon further quinidine therapy and to establish and

maintain digitalization. In such cases digitalization usually supports a satisfactory circulation and keeps the patient in a good enough state of health without the bother of frequent courses of quinidine and the annoyance of frequent shifting of the heart beat from normal rhythm to atrial fibrillation and back again. However not infrequently digitalis and quinidine are helpfully given together the former to help to maintain an improved myocardial tone and to prevent much tachycardia when atrial fibrillation occurs, and the latter to reduce the frequency of paroxysms of atrial fibrillation or to prevent them altogether

3 *Other measures of treatment of atrial fibrillation* are of less importance than is the use of digitalis and quinidine nevertheless some measures are useful and often necessary Avoidance of unnecessary physical and mental strain, fatigue, infections, overeating, and intemperate use of tobacco, tea, coffee, and alcohol (small amounts of these are often permissible) should always be a matter of routine even though the atrial fibrillation is the only abnormality The more trouble of other sort there is, especially in the form of heart disease and failure, the greater naturally must be the limitation imposed on the patient. Exercise, if possible, should be encouraged in mild form especially walking, but it is to be remembered that although the heart rhythm no longer originates in the sinoatrial node the heart rate is still subject to outside influences, apparently through nerve action on atrioventricular conduction. Excitement and exertion will increase the heart rate in spite of digitalis, even more than is the case in normal rhythm.

Special restrictions and special diets for atrial fibrillation are unnecessary Other drugs than quinidine and digitalis are also as a rule, unnecessary Synthetic quinidine and dihydroquinidine are effective but not superior to commercial quinidine while quinine is much less effective (Alexander et al 1947) strophanthus, squill, apocynum and convallaria may be effective in the manner of digitalis, but they are inferior members of the digitalis group, except in the case of strophanthin or ouabain, which is more potent than is necessary and may be actually dangerous if given in large or often-repeated doses—its use is much better limited to emergency treatment of congestive failure

In recent years two other drugs have been introduced as substitutes for quinidine in trying to abolish atrial fibrillation fagarine from South America (Deulofeu, et al., 1945 Taquini, 1947 Scherf, et al. 1949) and atabrine (Gertler and Yohalem 1949) both have been effective to some degree but need further study Incidentally fagarine can cause serious ventricular irritation.

Symptomatic treatment and the therapy of complications or of other conditions associated with atrial fibrillation should be carried out with little or no regard to the arrhythmia.

Surgical operations and anesthesia should not be withheld when they are obviously necessary procedures the atrial fibrillation is not a contraindication to their execution although it is always wise to control the heart rate or the

arrhythmia first by the use of digitalis or quinidine. It is essential to remember that thyrotoxicosis is an important cause of atrial fibrillation and that it may be difficult or impossible to control this arrhythmia until the thyrotoxicosis itself is corrected either surgically or medically It has been also of much interest, with thyrotoxicosis present, to observe the calming influence on the heart rate either in normal rhythm or in atrial fibrillation, of the administration of iodine for a short time in preparation for operation (for example, 5 gr of potassium iodide or 5 drops of Lugol's solution three times a day for a week) The discovery of this effect was made accidentally by Trousseau many years ago (1863) when he gave by mistake a prescription for tincture of iodine instead of tincture of digitalis to a patient with thyrotoxicosis and tachycardia. The heart rate was reduced much more readily by the iodine than by the digitalis which was later substituted on discovery of the original error

For the discomfort due to the palpitation induced by atrial fibrillation, either in paroxysmal or in permanent form, various medicines may be helpful, in particular bromides (for example, 1 gm [15 gr] of the triple bromides in solution two or three times a day for a few days as needed) Codeine and morphine should rarely be employed, and then only to tide over some exceptionally severe period of palpitation and associated discomfort or pain, especially when the tachycardia produces pulmonary edema or the status anginosus, before digitalis or quinidine becomes effective. Since paroxysmal atrial fibrillation is commonly recurrent, there is a real danger of habit formation (morphinism) in the use of the opiates.

B **Therapy directed to prevent paroxysms of atrial fibrillation or recurrence of "permanent" arrhythmia** is much like that already outlined for the prevention of paroxysms of tachycardia in Chapter 32. In the first place, factors that irritate the heart or nervous system and favor the onset of atrial fibrillation should be prevented, or at least reduced to a minimum such factors include nervous excitement and fatigue, sudden violent effort, prolonged exhausting exertion, hearty meals, excess of tobacco, alcohol, tea, or coffee, worry and late hours. Secondly there may be conditions of ill health which favor the appearance or persistence of atrial fibrillation, such as focal infections, general diseases, local strain of muscles or joints, painful conditions like stones in kidney or gallbladder and heart failure. These conditions should be corrected so far as possible, but not too abruptly or vigorously Thirdly there is more or less specific therapy possible by the administration of quinidine sulfate in daily rations of 0.2 to 0 4 gm (3 to 6 gr) once twice, three or four times a day according to need, constantly for a few doses, or for days at a time. Often such quinidine therapy is successful, at least in reducing the number and duration of the paroxysms of atrial fibrillation even if not in completely preventing them. It is a common experience that patients who have numerous long paroxysms, each lasting twelve to twenty-four hours or more and coming as often as once or twice a week, find that the attacks become infrequent and short under quinidine therapy lasting but two or three hours each time and coming perhaps once or twice a month. Finally when quinidine sulfate rations

are ineffective, it is wise to try the effect of digitalization and its maintenance. In rare cases digitalis seems to reduce the number and duration of the paroxysms, but its chief advantages lie in the facts (1) that when atrial fibrillation does occur depression of atrioventricular conduction already exists as the result of the digitalis effect and so the ventricular rate rises less than without digitalization, and (2) that digitalis tends to maintain atrial fibrillation as a permanent disorder of rhythm after it has recurred paroxysmally and so with its simultaneous control of the ventricular rate permits a much pleasanter existence than when atrial fibrillation is constantly coming and going. Sometimes quinidine and digitalis may be combined successfully in preventive therapy but if in spite of these drugs there is much discomfort from recurring attacks of atrial fibrillation other medicines, especially the bromides or phenobarbital, may prove useful in reducing the distress. The bromides should be used cautiously to avoid a toxic effect.

Protection of the heart from disturbing arrhythmias during surgical operations on and about the heart has been accomplished by the preoperative use of quinidine sulfate and the administration of procaine to the exposed heart or by intrapericardial injection, but the degree of effectiveness of these procedures has not yet been fully determined. In lung surgery too, quinidine given preoperatively may prevent arrhythmias.

Reassurance, so far as the atrial fibrillation is concerned, is almost always an important part of the therapy but the significance of the condition must not be minimized to the extent that the patient neglects necessary treatment.

Differential diagnosis. Atrial fibrillation has to be differentiated from gross sinus arrhythmia, multiple premature beats, paroxysmal tachycardia, and atrial flutter The most important point in differentiation of atrial fibrillation from any of these other disturbances of rhythm is the absolute irregularity of its rhythm, which is almost invariably present and rarely simulated by any other condition. If one is in doubt, resort may be had to exercise or to the increase in rate produced by amyl nitrite or atropine such procedures usually abolish the arrhythmia of sinoatrial or premature beat origin and increase that of atrial fibrillation. Besides differing from atrial flutter and paroxysmal tachycardia in rhythm, atrial fibrillation differs from these disorders further in that it is more often a permanent and less often a paroxysmal state, and in that it more often occurs with definite indications of organic heart disease also it more readily responds to quinidine and digitalis therapy

ATRIAL FLUTTER

Atrial flutter due to a disorder of atrial mechanism closely related to that of fibrillation but usually with regular rapid ventricular action, is uncommon; it was named by Jolly and Ritchie in 1911

Incidence. Atrial flutter is probably not so rare as statistics indicate since shorter paroxysms may easily be missed or considered to be paroxysmal tachycardia in the absence of graphic records. When it is recognizable without

graphic records, atrial flutter is found only about twice to every fifty cases of atrial fibrillation. When electrocardiograms are routinely taken, atrial flutter is found about once for every 14 cases of atrial fibrillation. Thus we found 104 cases of atrial flutter and 1 422 cases of atrial fibrillation among 10 000 patients electrocardiographed at the Massachusetts General Hospital from 1914 to 1931 (White and Sprague, 1931)

Mechanism (abnormal physiology) Atrial flutter is characterized by regular but abnormal atrial contractions at a very rapid rate, and usually by regular ventricular contractions at one half the atrial rate. The atrial rate ranges from 200 or slightly less to 400 or slightly more, with an average of 300 per minute. The ventricular rate is often exactly one half the atrial rate because of 2 to 1 atrioventricular block sometimes it is slower than that, or irregular due to greater or varying grades of block and rarely it is the same as the atrial rate due to the absence of block, this last-mentioned state often being called "1 to 1 rhythm. Generally conduction within the ventricles themselves is normal, but with very rapid rates functional intraventricular (bundle branch) block may occur disappearing later when the rate falls or the atrial flutter stops. Very rarely complete heart block may be associated with atrial flutter

The mechanism of atrial flutter is not yet perfectly clear Like atrial fibrillation, flutter has been for many years ascribed to a circus movement (Lewis, et al 1920) but recently doubt has been cast on this mechanism as noted earlier in this chapter (Scherf et al. 1948 Prinzmetal, et al. 1949) (see page 896) and an alternative proposed of rapid excitation from an irritable focus in the atria, as in paroxysmal tachycardia. If the path is shortened or its speed increased the atrial rate per minute increases and if this exceeds 400 per minute it becomes irregular When the excitatory process becomes very rapid and irregular it is no longer called atrial flutter but atrial fibrillation there is a wide boundary between the two clear-cut conditions which may be termed "flutter-fibrillation." Although atrial flutter and atrial fibrillation are closely allied in mechanism, their separation is useful and important from the clinical standpoint.

Atrial flutter has sometimes been regarded clinically as midway between atrial paroxysmal tachycardia and atrial fibrillation but it is much more closely related to the latter as evidenced, for example, by the electrocardiogram, which in the case of atrial flutter shows constant movement of the baseline due to atrial activity (Figure 159) while in atrial paroxysmal tachycardia there are short atrial waves sharply differentiated and separated from each other (Figure 156, page 879)

Atrial flutter like fibrillation, may be paroxysmal or permanent, it is much more likely to be paroxysmal, the paroxysms lasting usually for hours to days, occasionally for weeks, and rarely for months or years. Paroxysmal atrial flutter occurs in three or four times as many cases as does permanent atrial flutter

Etiology *Cause* The precise way in which atrial flutter is started is not clear but predisposing conditions are for the most part known. Like atrial

fibrillation atrial flutter is more commonly found in the presence of heart disease than in its absence. It is especially likely to occur in mitral stenosis, hypertension, thyrotoxicosis, and coronary heart disease, but it exists sometimes alone with no evidence of heart disease or any other pathologic condition. An otherwise perfectly healthy strong person may have atrial flutter. Whether it is the only abnormality or one associated with serious disease, it is commonly precipitated by sudden effort, nervous excitement, trauma, or surgical operation, particularly involving the thorax rarely it begins without apparent provocation.

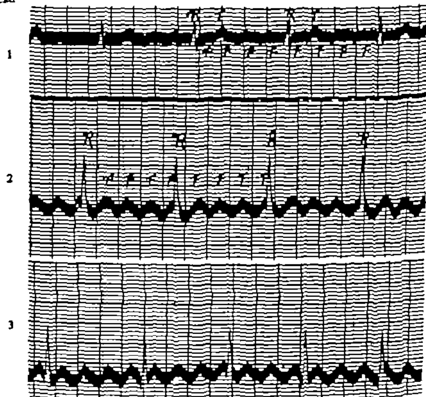


FIG. 159 Electrocardiogram showing atrial flutter Three leads. Four to one and three to one atrioventricular block.

In a series of 52 cases of atrial flutter observed by Parkinson and Bedford (1927) between the years 1913 and 1926 there were the following etiologic findings chronic rheumatic heart disease in 14 cases (27 per cent) acute rheumatic infection in 2 cases, other acute febrile illnesses in 3 thyrotoxicosis in 2, hypertension in 6, myocardial infarction in 3 a positive Wassermann reaction in 3 cardiac enlargement other than rheumatic, hypertensive, or syphilitic in 13 congenital heart disease in 1 and no evidence of heart disease in 5 Of the 14 cases of chronic rheumatic heart disease, 7 showed mitral

stenosis alone, 4 mitral stenosis and aortic regurgitation, 2 mitral disease without clinical evidence of stenosis, and 1 aortic regurgitation alone.

Sex The sexes are represented unequally in statistics so far available, the male sex preponderating in about the ratio of 3 to 1 The cause for this difference is not clear except that the male sex is generally under greater strain than the female sex.

Age The incidence of atrial flutter is much greater in later decades of life than in youth, three fourths of the cases occurring after the age of forty years. However it is encountered in children and even in infants.

Pathology There are no known structural changes in the myocardium characteristic of atrial flutter There may be extensive heart disease or there may be none· the abnormal finding more often noted than any other in a heart with atrial flutter is mitral stenosis.

Symptoms. The typical symptom of atrial flutter is rapid, regular forceful palpitation, sometimes described by the patient himself as heart flutter but not distinguishable in sensation from paroxysmal tachycardia. There may or may not be symptoms of congestive failure coincident with, or in some cases induced by the atrial flutter· congestive failure is likely to occur if the atrial flutter is of long duration in persons with damaged hearts. Pain is rare precordial aching may occur The alarm occasioned by the atrial flutter may be so great that much nervous excitement and even a state of nervous prostration may exist. If the ventricular rate is very rapid, as sometimes happens when there is no block (1 1 rhythm) and the heart rate approaches 300 per minute, weakness, dizziness, faintness, or even actual syncope may occur associated with cerebral anemia and other effects of the very small output of blood and much reduced blood flow

Signs. The characteristic sign of atrial flutter is the regular rapid heart rate, which is maintained, often with variations of but a few beats from minute to minute, for days, weeks, or months at a time, in spite of exercise, rest, and sometimes even drug therapy The apex rate and usually also the radial pulse rate average about 150 per minute, while electrocardiograms show double this rate for the atrial action (about 300 per minute) in approximately half of the cases of atrial flutter when first seen. Sometimes the heart rate is found to be irregular even before treatment, due to varying grades of block, usually 1 1 2 1 3 1 or 4 1 coming in regular or quite irregular sequences, so that the arrhythmia may be an orderly one or a very disorderly one. Sometimes the heart rate is regular and very fast (with 1 1 rhythm) or regular and slow (with 3 1 4 1 6 1 or even 8 1 block regularly maintained) These variations of block thus account for that half of the cases of atrial flutter without a constant 2 to 1 block. Although great and irregular variation of grades of atrioventricular block may produce a heart action that seems on cardiac auscultation or on palpation of the pulse to be absolutely irregular careful study and especially measurement of the arteriogram will show the existence of a dominant rhythm, whereby for example, four pulse intervals of 2 to 1 block will equal in duration two pulse intervals of 4 to 1 block· this finding of a definite

dominant rhythm rules out atrial fibrillation, even without an electrocardiogram, but the measurements are sometimes difficult and obscure. Some cases that happen to have atrial flutter with an atrial rate of about 300 and 4 to 1 heart block, which occurs either spontaneously or after treatment, are almost sure to escape notice clinically because of their regular slow heart action and pulse rate of about 75 unless phlebograms or electrocardiograms are taken. This infrequent but important happening is a further illustration of the value of graphic records (see Figure 159 page 914)

Related to the natural tendency for atrial flutter to show a v block is a clinical test for this disorder of rhythm. It is the rule for firm pressure by the fingers over the carotid sinus on either side of the neck to increase the grade of block and so to slow the heart rate to one half or even less during the application of the pressure, the fast and regular rate quickly returning on release of the pressure to its original high level. Thus a ventricular rate of 150 with 2 to 1 block in atrial flutter can drop to 75 with the change to 4 to 1 block. Such a change does not occur in sinus tachycardia, while if a sharp drop of heart rate occurs in the case of atrial paroxysmal tachycardia when pressure is applied to the carotid sinus, it means that the paroxysm has been abolished and so the rate does not go up again directly the carotid sinus pressure is released.

In doubtful cases when atrial flutter is possible or suspected, electrocardiograms should be obtained they are far superior to clinical signs or tests and to phlebograms because they not only reveal the atrial action more clearly but they distinguish at once between atrial flutter and atrial paroxysmal tachycardia, and, moreover they afford other information about the cardiac mechanism. The flutter waves produced in the electrocardiogram by the atrial action are best shown by a special lead with exploring electrode over the third intercostal space just to the right of the sternum they are almost always well seen in Leads 2 and 3 but are often so poorly marked in Lead 1 and in the routine precordial leads over the right and left ventricles (V_1 to V_6 inclusive) that the interpretation from these leads may remain in doubt.

Roentgen ray study in atrial flutter is of relatively little value, although in some cases the abnormal mechanism may be observed fluoroscopically

With atrial flutter there may or may not be signs of cardiac enlargement, valvular disease, pericarditis, aortic disease, hypertension, or congestive failure in half the cases or more there are such signs.

Special tests may show a decreased blood flow when the heart rate is very rapid, but this will return to normal when the ventricular rate falls, if there is no heart failure. With very fast heart rates the systolic blood pressure also tends to be low (100 mm or less) and the pulse pressure small (20 to 30 mm)

Course and prognosis. Clinically atrial flutter falls midway between atrial paroxysmal tachycardia and atrial fibrillation as regards significance and duration. It is more important than paroxysmal tachycardia, because it is found more often with heart disease and lasts longer but it is somewhat easier to

control. It is somewhat less important than atrial fibrillation, because it is less often permanent and is less likely to be associated with serious heart disease; the heart rate is, however harder to control. Generally atrial flutter lasts for hours, days, or weeks, rarely for minutes, months, or years. We have observed an instance of atrial flutter lasting five years with ventricular rate for most of the time at 130 per minute (2 to 1 atrioventricular block) or 260 (1 1 rhythm) not responding to treatment but stopping spontaneously and leaving no trace of heart disease (Sprague and White, 1928) Lewis has known atrial flutter to last uninterruptedly for twenty-four years, the ventricles beating without cessation at 140 per minute (Lewis, 1937) and Kossman and Berger (1941) have reported an instance of eleven years duration we have had another case under our own observation for twenty-six years who is still in good health with no other evidence of heart trouble than the preexistent atrial flutter

The condition starts abruptly and usually either stops abruptly or changes suddenly or slowly to atrial fibrillation, the ventricular rate usually falls through increase of the grade of heart block under digitalis therapy It often is a disagreeable and more or less crippling condition, but it is rarely dangerous. In a few cases, generally with serious heart disease, atrial flutter of long duration and not yielding to treatment leads to heart failure and may even cause death.

Complications. Congestive heart failure, atrial thrombosis, and embolism may occur as complications of atrial flutter but they are less common than in the case of atrial fibrillation.

Treatment. Atrial flutter is more amenable to digitalis therapy than to quinidine therapy and it is wiser to use digitalis than any other drug in the treatment of established flutter *If there is but a brief paroxysm lasting a few minutes or at most a few hours,* no treatment at all may be necessary other than rest and reassurance.

When atrial flutter has lasted for more than a few hours, digitalis therapy should be started, preferably 0.2 gm (3 gr) of the standardized powdered leaf or digitoxin 0.2 to 0 3 mg by mouth, three times a day for two or three days as needed. In emergencies when the tachycardia associated with the flutter causes great distress or myocardial failure, the digitalis can, of course, be given intravenously as described for atrial fibrillation earlier in this chapter (see page 905) If the atrial flutter persists after three days but the ventricular rate has been reduced to normal figures by increase in the grade of block (4 to 1 or more) the digitalis leaf may be reduced to a daily ration of 0 06 or 0 1 gm (1 or 1½ gr) or the digitoxin to 0 1 to 0.2 perhaps best 0 15 mg, to maintain the full drug effect so long as is necessary If atrial fibrillation has been induced, the digitalis may be continued to maintain a slow ventricular rate or it may be dropped to see whether or not normal rhythm will soon follow as it sometimes does this latter was once thought to be the usual ("classical") course When normal rhythm does return, the continuance of

treatment is not necessary except for the avoidance of factors which may induce a return of the atrial flutter and a prophylactic dose of quinidine sulfate 0 2 gm (3 gr) four times a day for a few days may be used.

Quinidine sulfate may be administered, in the way described for atrial fibrillation earlier in this chapter to cases not responding to digitalis or to cases believed amenable to quinidine for the purpose of restoring normal rhythm at the outset or after the atrial fibrillation into which it is converted has become fixed, whether or not there is a slowing of the heart rate by digitalis.

In about half the cases of atrial flutter digitalis therapy is successful, in another few cases quinidine is successful when digitalis fails, in others digitalis is partly successful in that a satisfactorily slow heart rate is produced although atrial flutter or fibrillation continues, and in rare cases neither digitalis nor quinidine controls either the atrial mechanism or the ventricular rate, the attack of flutter stopping spontaneously perhaps after months or even years The best course generally to pursue is first to digitalize the patient with atrial flutter and then, if normal rhythm is not restored, to try a course of quinidine sulfate.

Complications of atrial flutter like congestive failure, demand treatment as much as does the disturbance of heart rhythm digitalis is especially valuable in this respect for it is the best therapy for both the atrial flutter and the congestive failure. If the situation is urgent, the drug may be given intravenously as stated above.

Finally to prevent paroxysms of atrial flutter or a recurrence of "permanent" flutter care should be taken to avoid exciting factors—fatigue, physical or mental, sudden exertion, overeating, excessive use of tobacco, alcohol, tea or coffee, infections, focal or general, unnecessary surgical operations, and congestive heart failure Rations of quinidine sulfate 0.2 gm (3 gr) three or four times a day or of digitalis 0 06 or 0 1 gm (1 or 1½ gr) daily after digitalization, are also sometimes effective, just as they are in reducing the number and duration of paroxysms of tachycardia or of atrial fibrillation such drugs should be used as needed, but not necessarily as a routine in every case.

Differential diagnosis. Atrial flutter is to be differentiated from sinoatrial tachycardia, paroxysmal tachycardia, and atrial fibrillation. Its long duration with rapid steady heart rate under various circumstances, the absence of fever thyrotoxicosis, and excitement, which might be responsible for sinoatrial tachycardia, and the frequent presence of heart disease help to distinguish atrial flutter from rapid normal rhythm. The long duration of the paroxysms of atrial flutter the more common association with heart disease, and the tendency of carotid sinus pressure to slow the heart rate temporarily by increasing the grade of block but not to abolish the abnormal rhythm distinguish flutter clinically from paroxysmal tachycardia. The regularity of rhythm is the essential characteristic which ordinarily differentiates flutter from fibrillation. It is often necessary however and always wise to obtain an electrocardiogram to be sure of the diagnosis of atrial flutter

VENTRICULAR FIBRILLATION AND FLUTTER

Ventricular fibrillation consists of an apparently incoordinated ventricular action with cessation of regular contraction, resulting in death if effective ventricular action is not speedily resumed. It was first noted in 1850 by Hoffa and Ludwig in the laboratory. As a temporary or terminal condition it is frequently seen in experimental animals, as in the dog and cat, and it has occasionally been encountered in human electrocardiograms, in dying patients. It probably is commonly a terminal condition in man but an actual cause of death only under certain circumstances, as in fatalities resulting from the blocking of the coronary circulation and in death during chloroform anesthesia, from acute benzol poisoning, and from electrocution, which procedures have been shown to cause ventricular fibrillation in experimental animals and in rare instances in man. The smaller the heart in experimental animals, the greater the chance for restoration of normal rhythm; the human heart may be too large to permit frequent recovery even if ventricular fibrillation were of frequent occurrence.

A number of human electrocardiograms showing ventricular fibrillation have been published, but the separation electrocardiographically between ventricular fibrillation and ventricular paroxysmal tachycardia and flutter is not a sharp one and the interpretation is sometimes in doubt. A clear-cut instance is shown in Figure 160.



FIG. 160. Electrocardiograms of case with bundle branch block (*A*) who died in an attack of ventricular fibrillation (*B*). (Graybiel and White, *Electrocardiography in Practice*, 1941. Kindness of W. B. Saunders Company, Philadelphia.)

The mechanism of ventricular fibrillation is obscure. It may be similar for the ventricles to that of atrial fibrillation for the atria. It may consist of an irregular circus movement; or there may be multiple spread or foci of ventricular activity.

The relationship of the mechanisms of ventricular paroxysmal tachycardia and ventricular fibrillation seems close, the former tending to evolve into the latter via an intermediate mechanism, *ventricular flutter*, which has been discussed recently by Fastier and Smirk (1948) and which is very rapid but

regular One of the most authoritative opinions concerning the pathologic physiology or mechanism, of ventricular fibrillation is that presented by Wiggers in 1940 After stating that the process is an evolution of changes from the moment of its inception until it ceases completely in the course of 30 to 45 minutes, Wiggers writes that "the available evidence favors the conclusion that, after a single premature systole, the phenomenon is caused by re-entry of circulating wave fronts which involve smaller and smaller blocks of myocardium, each of which develops an independent excitation. As a result of the anoxia which develops progressively after the cessation of coronary flow conduction is slowed and the vigor of fractionate contractions decreased. The resultant of these changes causes, in succession, the undulatory convulsive, tremulous, and atonic stages of its evolution." Wiggers has been able to carry out "defibrillation" experimentally in dogs by passing strong alternating currents for brief intervals of 0 1 to 5 seconds through the ventricles, provided such countershock is applied within approximately two minutes. Application of comparable electric shock by chest electrodes to man would, Wiggers states, be dangerous to both operator and patient. Massage of the heart in the case of dogs with more prolonged asystole has aided in the recovery of the heart by the countershocks

Clinically ventricular fibrillation and flutter are conditions of uncertain importance in the present state of our knowledge They have been encountered after massive doses of digitalis and after epinephrine (adrenaline) as an end stage of ventricular paroxysmal tachycardia, and in a few patients dying with other conditions. They are probably commonly a terminal event after coronary thrombosis and during chloroform anesthesia and electrocution. They are also a hazard in cyclopropane anesthesia. They have been noted in rare cases dying of angina pectoris while being electrocardiographed, and have been found in individuals dying of some infectious diseases. However they are not the only mechanism of heart death, depression of the pacemakers and of atrioventricular conduction being found more often. Syncope, transient or leading to death, and simulating the Adams Stokes syndrome, has been reported in several cases of prolonged ventricular fibrillation It is always very ominous. Recovery has been rare.

It is probable that quinidine sulfate does help to prevent fibrillation of the ventricles if given in moderate dosage to individuals threatened with this usually fatal arrhythmia, especially in cases of recent myocardial infarction or those subject to paroxysms of ventricular tachycardia, but as yet we have no certainty of this Borg (1939) suggested its use in all cases of coronary insufficiency and believes that he reduced the mortality in coronary heart disease thereby My own experience makes me think that he is right, but adequate statistical proof is still lacking. Acetylcholin (acetyl-B-methylcholin chloride) and papaverine have been shown in experimental animals to act prophylactically (Nahum and Hoff, 1934 and Lindner and Katz, 1941 respectively)

In the last edition of this book it was stated that there was no specific

therapy once ventricular fibrillation has begun. However Beck et al. (1941 and 1947) have demonstrated that if the heart is exposed an electric shock of 110 volts and 1 15 amperes can restore the normal heartbeat. They have reported success in one case of ventricular fibrillation of long duration.

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CHAPTER 34

BRADYCARDIA AND HEART BLOCK (SINOATRIAL, ATRIOVENTRICULAR, AND INTRAVENTRICULAR) VENTRICULAR ESCAPE. ATRIOVENTRICULAR NODAL RHYTHM. SUDDEN DEATH

Heart block in its various manifestations, the subject of the present chapter is primarily the result of depression of the specialized tissues that normally initiate the heartbeat (sinoatrial and atrioventricular nodes) and conduct it to the muscle of both ventricles (atrioventricular bundle and its branches) In contrast to the abnormal cardiac rhythms due to unusual excitability and stimulation that have been considered in the last two chapters. When the sinoatrial node is much depressed we have *sinoatrial block* often with control of the heartbeat by the atrioventricular node If this lower nodal pacemaker initiates occasional beats we speak of *ventricular escape* if it controls the ventricular rhythm entirely we speak of an *idioventricular rhythm*, and when it controls atrial as well as ventricular action, with sinoatrial node wholly silent, we speak of *atrioventricular nodal rhythm.* Delay or more or less complete blocking of the impulse (initiated by the sinoatrial node) in the atrioventricular node and bundle gives rise to *atrioventricular block* while delay or blocking of the impulse in the bundle branches causes *intraventricular block* or *bundle branch block* The immediate causes (mechanisms) of sudden death are (1) complete depression of both nodes, (2) a complete blocking of the atrial impulse above the ventricular muscle with paralysis of the lower nodal and bundle pacemaker and (3) ventricular fibrillation (see Chapter 33 for this last-named disorder)

SINOATRIAL BRADYCARDIA. SINUS ARRHYTHMIA AND BLOCK. ATRIAL STANDSTILL. VENTRICULAR ESCAPE

Mechanism. If the normal pacemaker the sinoatrial node is depressed the heart rate slows *sinoatrial bradycardia* is the term applied to this slowing of

the whole heart. Often associated with the bradycardia is *sinus arrhythmia* (Figure 161A). If it happens that occasionally or frequently there appears between atrial beats an interval which is equal or almost equal to two usual cycles, the condition is called *partial sinoatrial block*. If the atrial rate becomes very slow (35 or less per minute), whether regular (as it usually is) or irregular, the condition is sometimes termed high-grade sinoatrial block; and if the atrial contractions drop out altogether, the ventricles continuing to beat as the result of independent stimulation from the atrioventricular node, a condition results which has been called *complete sinoatrial block*, *atrial standstill*, or *atrial paralysis*.

Incidence. *Sinoatrial bradycardia* is normal and unimportant except when of extreme degree, that is, when the whole heart rate sinks below 35 or less per minute. A sinoatrial rate of 50 or 60 is common in many normal individuals at rest, sometimes during sleep or on first waking in the morning the heart rate may be as slow as 45. Sinoatrial bradycardia can frequently be produced by *vagal stimulation*, most readily by pressure over the right *carotid sinus* in normal persons or in patients whose heart rate is already rather slow, and especially if digitalis has been previously given in moderate or large dosage. Occasionally in a normal person carotid sinus pressure may slow the heart excessively, and faintness and even syncope have been caused by such tests, especially if the carotid sinus is sensitive. If the pulse is fast, usually because of sympathetic nerve stimulation, carotid sinus pressure is much less effective, except in a few cases when it may abolish paroxysmal tachycardia or increase the grade of heart block already present in atrial flutter. Pressure on the left side of the neck and on the eyeballs (oculocardiac reflex) may also slow the heart by causing depression of the sinoatrial pacemaker through vagal stimulation, but pressure in such places is usually less effective than right carotid sinus pressure. Voluntary slowing, unlike voluntary acceleration, of the heart rate is not directly possible; the individuals who have been reported to have slowed their pulse voluntarily have apparently caused bradycardia reflexly by respiratory effort, or have obliterated their radial pulse by muscular movements of the thorax, mainly by an upward and backward shrugging of the shoulders, thereby compressing the subclavian arteries. Athletes sometimes show an abrupt fall in heart rate, even a halving, shortly after the completion of some special effort; this apparently is a normal vagal reaction which tends to be much accentuated by training.

It is very important to remember that a heart rate in the forties or even in the thirties per minute at rest can be a perfectly normal occurrence, especially in athletes in training and particularly in distance runners (White, 1942).

Etiology. *Cause.* Pathologic degrees of sinoatrial bradycardia, block, and arrhythmia are seen rarely. They are most commonly produced by digitalis in excessive dosage and in individuals whose tolerance for the drug is low. Other drugs of the digitalis group and quinidine sulfate (and allied cinchona alkaloids) can also depress the sinoatrial node in high degree. Vagal irritation by excessively sensitive carotid sinus, by direct pressure of tumors, by infec-

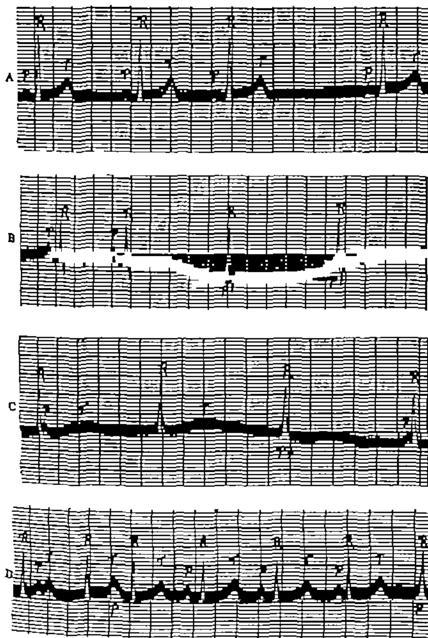


FIG. 161 Electrocardiograms (Lead 2) showing (*A*) sinus arrhythmia and bradycardia or block; (*B*) sinus arrhythmia with ventricular escape induced by deep breathing; (*C*) atrioventricular dissociation due to independent action of sinoatrial and atrioventricular pacemakers at almost the same rate (50 per minute) and (*D*) atrioventricular dissociation due to escape of the atrioventricular nodal pacemaker at a rate of 90 per minute.

tion in the neck or mediastinum, and by intracranial tumors and high intracranial tension has likewise been reported as a cause of sinoatrial block. Sometimes the heart abruptly ceases to contract during anesthesia or surgical operations. Heart disease itself is a very rare cause of sinoatrial block but obstruction of blood supply to the sinoatrial node by atheroma or occlusion of its artery has been thought responsible in a few cases. Lesser degrees of bradycardia with rates of 45 to 55 are occasionally found in certain diseases such as epidemic parotitis and jaundice of either infectious or obstructive origin, and sometimes during convalescence from any acute illness such as influenza.

The commonest of these conditions is simple sinoatrial slowing with regular heart action at rates of 30 to 40· less often there is gross sinus arrhythmia at these rates the dropped beat is rare and least common of all is complete atrial standstill.

Both *sexes* and all *ages* are subject to these disorders of the sinoatrial mechanism but they are more common in youth. It was once thought that well-marked sinus arrhythmia was a sign of a healthy heart this is not so, but it is true that in the absence of some special cause, like a digitalis effect, it is found more often in youth than in old age and it is abolished by the sympathetic stimulation that comes with infection, for example, rheumatic infection. To this extent, then, sinus arrhythmia is a sign of a healthy heart, in that heart disease is less common in youth than in old age and less common in young persons without active infection than in those with such infection, especially in a rheumatic environment. There is one exception to these remarks, for infrequently in elderly persons with arteriosclerosis or heart disease a considerable degree of sinus arrhythmia may be found as a distinctly abnormal sign (Faulkner 1930)

Symptoms. There are no particular symptoms of sinoatrial bradycardia. If the rate is very slow or irregular there may be disagreeable palpitation or even weakness, dizziness, and syncope when the periods of standstill are prolonged. In fact, the marked slowing of the pulse, with syncope and convulsions that may rarely result from extreme sinoatrial nodal depression, is indistinguishable from the Morgagni Adams-Stokes syndrome found with atrioventricular block, unless graphic records are taken. Symptoms of congestive failure are rare. Nervous symptoms are common, for the subjects of sinoatrial nodal depression may also have neurocirculatory asthenia.

Signs. The one sign of sinoatrial depression is the slow heart rate originating in the atria (Figure 161A, page 927) There may or may not be arrhythmia, but it is rarely absolute, so that there is little likelihood of confusion between atrial fibrillation with atrioventricular block and sinoatrial depression. When there is doubt an exercise test will make the pulse more regular in the case of sinoatrial arrhythmia and bradycardia, with increase in rate, while the pulse in atrial fibrillation will become more irregular There may or may not be signs of heart disease, heart failure, or hypertension. Roentgen ray study is of little or no value. Electrocardiography affords the greatest aid, for it usually reveals

at a glance the abnormal mechanism and the relationship of atrial and ventricular activities (Figure 161)

At times in sinoatrial bradycardia the electrocardiogram shows that there is not always a *normal atrioventricular sequence* The atrial rate may be so slow that the idioventricular pacemaker in the atrioventricular node does not wait for the impulse from the sinoatrial node, but escapes. Such *ventricular escape* may be for one beat only or it may be for a group of beats (Figures 161B C, and D page 927) or if the atria are wholly paralyzed, it may constitute the entire cardiac mechanism (Figure 162) Ventricular escape is of no particular clinical significance but it constitutes an interesting physiologic adjustment of the body in case of need. It sometimes has been confused with heart block and so labeled wrongly it is, to be sure, atrioventricular dissociation, but it is not atrioventricular block. It has sometimes been called *interference dissociation*, when both nodes are active without true heart block (Figure 161D)

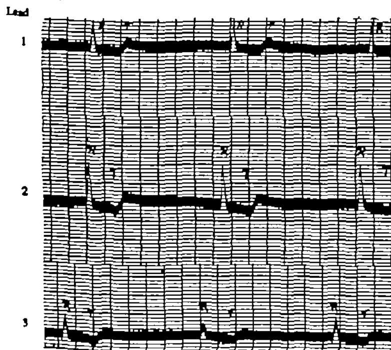


FIG. 162. Electrocardiogram showing atrial standstill. No evidence of *P* waves in any of the three leads. Digitalis inversion of *S-T* segments and *T* waves. A jugular phlebogram also failed to show any evidence of atrial activity in this case.

The course, complications, and prognosis of disturbances of sinoatrial rhythm due to depression are generally of little clinical importance. As a rule the condition is a *transient* anomaly perhaps surprising and sometimes disagreeable but only rarely dangerous. In extreme cases there may be syncope and even death, due probably to paralysis of the ventricular pacemaker also,

as with poisoning by quinidine or digitalis and with sudden standstill of the heart during anesthesia and surgical operations.

The treatment consists of the omission of the toxic agent, for example, digitalis or quinidine, or of the control of other underlying cause, such as cerebral disease. For marked bradycardia with faintness or syncope, drugs may be needed atropine sulfate, 1 mg (1/60 gr) or more subcutaneously every four hours as needed, if vagal stimulation is the chief factor otherwise epinephrine (adrenaline) or ephedrine Epinephrine hydrochloride may be given subcutaneously intravenously or even into or over the heart directly to stimulate a resumption of normal beating. Life has apparently been saved in a number of cases by the intracardiac injection of 0 5 cc or less of a 1 1,000 solution of epinephrine hydrochloride after the heart has stopped beating during anesthesia and surgical operations or obstetric procedures, or in smaller dosage (0 1 cc) in stillborn infants This is an emergency treatment which should always be borne in mind, and although it may often prove fruitless, an occasional rescue makes it of decided value Cardiac massage when possible is, however much more effective and wiser than the use of drugs, and steps should more often be taken to carry it out to save lives otherwise doomed; artificial respiration should be carried on simultaneously If serious heart disease is back of the cardiac standstill resuscitation by any method is very unlikely to succeed cardiac massage and electric shocks plus artificial respiration may conceivably be successful even in such cases but the difficulties of carrying out this therapy are almost always insurmountable

Ephedrine hydrochloride may be given in the dosage of ¼ to ½ gr (15 to 30 mg) by mouth three or four times a day instead of epinephrine, as prophylaxis against cardiac standstill but it is much less likely to be effective; the same statement applies in general, though to a lesser degree, to the more recently introduced Paredrine, given in the dosage of 40 to 60 mg by mouth three times daily (Nathanson, et al. 1942)

If an excessive sensitiveness of the carotid sinus on either side is found as a basis for syncopal attacks a cure can be effected by carotid denervation, but it is very important first to rule out atrioventricular block revealed or increased by the effect of a normal carotid sinus reflex.

For lesser grades of sinoatrial bradycardia, block, and arrhythmia no treatment at all is necessary The importance of the condition is often overemphasized and reassurance is more needed than anything else, with discontinuance of various unnecessary remedies At times the most useful of all measures is electrocardiography to establish the diagnosis of an unimportant sinus arrhythmia or bradycardia and to rule out atrioventricular block, which perhaps had been suspected as an aftermath of some serious infection such as influenza or pneumonia. Almost invariably the supposed heart block present during convalescence from some important infectious disease proves to be merely sinoatrial bradycardia.

Intra-atrial block that is, defective conduction of the wave of excitation and contraction through the atrial muscle itself has been produced and studied

in experimental animals It may be caused by certain poisons, such as quinidine sulfate and digitalis, and by vagal stimulation. When of high degree the excitation wave may be so diverted as to alter the shape of the *P* wave of the electrocardiogram. Its existence in man has been indicated by variations in shape and rhythm of the atrial waves of the electrocardiogram, for example, during quinidine therapy but its clinical importance has not been established except in atrial flutter and atrial fibrillation.

Interatrial block partial and complete, has been produced and studied in experimental animals, but its occurrence in man although suggested and described has not been conclusively proved. To effect independent action of the two atria very extensive structural or functional changes would be necessary to block off all the extensive muscle tracts joining the two atria.

ATRIOVENTRICULAR NODAL RHYTHM

A rare but interesting abnormal heart rhythm in man is that which originates in the atrioventricular node in the junctional tissues and controls both atrial and ventricular contractions. Atrioventricular nodal rhythm differs from ventricular escape and idioventricular rhythm only in that the atria as well as the ventricles are controlled by this lower pacemaker the sinoatrial node or other atrial pacemaker being superseded, at least for the time being. The obstinacy of the atrium in maintaining its own pacemaker accounts for the great rarity of atrioventricular nodal rhythm. Occasionally unusual irritation or irritability of the junctional tissues accounts for premature beats or paroxysmal tachycardia of atrioventricular nodal origin, but a steady rhythm at a slow rate arising from the junctional tissues is another matter and it is this that is called atrioventricular nodal rhythm (Figure 163 page 932)

Three conditions are necessary for the establishment, even for a short time, of atrioventricular nodal rhythm (1) marked depression of the normal pacemaker of the heart situated in the sinoatrial node and failure of any other part of the atrial muscle to assume its role, (2) normal activity (potential or latent ordinarily) of the pacemaking function of the atrioventricular node, and (3) ability of the impulse to pass backward from the junctional tissue into the atria to cause their contraction, that is, an absence of a state of reversed block. The rate of impulse formation in the atrioventricular node averages in man about 40 per minute, with a range of 30 to 50 and that heart rate therefore is usual in atrioventricular nodal rhythm. The heart action is as a rule quite regular sometimes absolutely so but at times there is more or less irregularity as in the case of sinus arrhythmia, due to vagus and sympathetic nerve action on the junctional tissues. It is at times possible by vagal stimulation or through the action of digitalis to depress the reversed conduction to the atria and so to delay the ventriculoatrial interval, and even block off the atrial response altogether that there may be atrial standstill with persistence of ventricular action (idioventricular rhythm) (Figure 162, page 929) Release of vagal inhibition by atropine, or sympathetic stimulation by exercise,

may first shorten the ventriculoatrial conduction time and then restore sinoatrial nodal function and normal heart rhythm.

Atrioventricular nodal rhythm is a rare clinical condition It is unimportant, except that it should be differentiated from the more serious disturbance of heart block. It can be studied satisfactorily only by electrocardiogram, although a phlebogram from the jugular pulse may indicate its presence. Inspection of the jugular pulse (without a tracing) and fluoroscopic observation of the superior vena cava may show a very prominent pulsation, due to coincidence of atrial and ventricular contractions, suggesting this unusual rhythm; but confirmation by electrocardiogram is necessary Any uniformly regular pulse at a rate of 35 to 40 per minute should be investigated to learn whether it is due to atrioventricular block (most likely) to sinus bradycardia (less

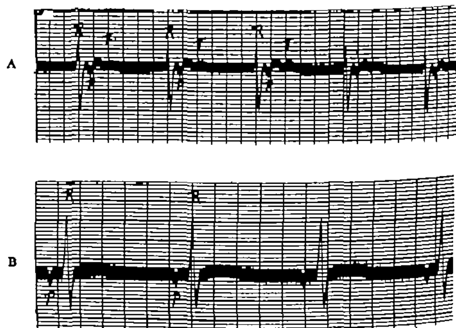


FIG. 163 Electrocardiograms (Lead 2) showing atrioventricular nodal rhythm. Two types (*A*) with *P* wave following the *QRS* wave, and (*B*) with the *P* wave preceding the *QRS* wave.

likely) or to atrioventricular rhythm (rare) As a rule in atrioventricular nodal rhythm the atrial contraction follows the ventricular contraction, less often it coincides exactly with it, and very infrequently precedes it (Figure 162) The *P* wave in the electrocardiogram is usually inverted and found at an interval of 0 1 to 0 2 second after the onset of the *QRS* wave It has been described as upright in rare cases, due to an unusual position of the atria or unusual course of the excitation wave in the atria in relation to the axis of Lead 2 of the electrocardiogram. If the atrial contraction follows the ventricular by a considerable interval, usually over 0 2 second, a second ventricular

contraction may in turn follow the atrial contraction, producing a bigeminal heart action with one atrial contraction between two ventricular beats. This is a rare phenomenon that has been noted in a few cases.

Unusual sinoatrial nodal depression from the effect of digitalis or other cause, generally unknown, has been responsible for the occasional cases of atrioventricular nodal rhythm seen clinically The diagnosis, usually an unexpected one, has been made by electrocardiogram. The condition is generally temporary or recurrent, lasting for a few beats, minutes, or hours at a time and alternating with normal rhythm rarely it lasts for weeks or months or as a recurring condition for years. There may or may not be heart disease associated with it, usually there is not. The prognosis is dependent on other findings and not on the atrioventricular nodal rhythm, which appears to be a harmless condition, not needing treatment in itself and not easily controlled by any special therapy

ATRIOVENTRICULAR BLOCK

Depression of the function of conduction of the atrioventricular node (of Tawara) and bundle (of His) which join atrial and ventricular muscle, results in delay or obstruction of the excitation wave as it travels downward from the atria to stimulate the ventricles. This delay in conduction has been called atrioventricular block, in early days it was known simply as *heart block* for it was the first kind of block to be recognized, being described long before the special tissue itself was discovered.

Incidence. Atrioventricular block is undoubtedly more common than statistics show for slight grades are easily and probably usually missed, inasmuch as electrocardiograms are taken of relatively few patients. The higher grades of atrioventricular block are, however certainly far less common than are premature beats, atrial paroxysmal tachycardia, and atrial fibrillation they are more common than atrial flutter and ventricular proxysmal tachycardia. In the fifteen years from 1916 to 1930 inclusive at the Massachusetts General Hospital in an electrocardiographic series of 10 000 patients with cardiac symptoms or signs atrioventricular block was diagnosed in 641 cases (6 4 per cent) The block was complete in 79 or 12 per cent of these 641 cases and partial in 562 or 88 per cent (296 of the 562 cases of partial block showed only a delayed *P-R* interval) In another series of 69 cases of atrioventricular block, coronary disease was apparently responsible in 35 (50 7 per cent) rheumatic infection in 19 (27.5 per cent) congenital defect in 1 syphilitic involvement in 1 digitalis medication in 9 and an unknown factor (probably congenital) in 4 cases (White and Jones, 1928) In another series of 74 cases, a congenital etiology was diagnosed in 14 per cent, rheumatic heart disease in 4 per cent, syphilis in 7 per cent, and other myocardial disease, probably coronary in type, in 75 per cent (Campbell, 1944)

Mechanism (abnormal physiology). Atrioventricular block or defective atrioventricular conduction is due to the failure of the atrioventricular node

and bundle to transmit the excitation wave at a normal rate from atria to ventricles because of destruction from disease or because of prolongation of the refractory period resulting from disease, faulty nutrition, vagus nerve action, or fatigue from excessive speed of stimulation, as in extreme tachycardia. Atrioventricular block is a more or less normal phenomenon in atrial fibrillation, atrial flutter and very rapid atrial paroxysmal tachycardia, when the atrial rate is so fast, over 200 and often over 300 per minute, that even perfectly normal atrioventricular junctional tissue cannot resume a responsive state between successive stimuli In such cases 2 to 1 or higher grades of block quite naturally are found In these patients such block is of no serious significance in fact it is actually helpful for the heart and circulation. Treatment of atrial fibrillation and atrial flutter consists chiefly of attempts to increase the grade of block in order to reduce the ventricular rate.

When however at normal or only moderately accelerated speed of atrial activity there is delay or obstruction to the passage of the impulse to the ventricles, an important type of atrioventricular block exists. Although the block may originate in any part of the short tract of junctional tissue between the atrial muscle and the bifurcation of the bundle into its two branches, which pass to right and left ventricles respectively and even in these branches themselves if both are affected, the most susceptible and probably one of the commonest sites of blocking is at the very point where atrial muscle enters the junctional tract this has been shown by animal experiments and clinical observations (Lewis, White, and Meakins, 1914 White, 1915) It appears likely that toxic and nervous influences act chiefly at this point, although destructive lesions are more common lower down, that is, in the bundle itself.

Atrioventricular block may be temporary and functional, or permanent and organic. It may be of all grades from very slight delay in conduction, so that the *P R* interval of the electrocardiogram measures 0.21 second, to complete block when no impulses at all pass through from atria to ventricles. Any defect in atrioventricular conduction short of complete dissociation is called partial heart block. By far the commonest of all grades of block are the lesser ones with simple delay in conduction without dropped beats (Figure 164) cases with such slight block usually pass unrecognized unless graphic records are taken. The *P R* interval in these cases varies from 0.21 up to 0.50 second or even longer but intervals of over 0 30 second are decidedly rare. Faulkner has reported a case in which the *P R* intervals actually exceeded the *R-R* intervals in duration (Faulkner 1935)

Occasional dropped beats and higher grades of partial block, in which every fourth atrial impulse is blocked (called 4 to 3 block, because there are four atrial contractions to three ventricular contractions) or every third impulse is blocked (3 to 2 block) or every second (2 to 1) or every second and third (3 to 1) are usually easily recognized clinically and can often be analyzed simply by careful auscultation of the heart and by inspection of the jugular pulse though more easily by electrocardiogram (Figure 164)

Grades of partial heart block higher than 2 to 1 are very rare although

3 to 1 (Figure 164C) 4 to 1 and even 5 and 6 to 1 do occur As a rule the pacemaker in the atrioventricular node escapes and establishes an independent ventricular or idioventricular rhythm if the grade of block becomes greater than 2 to 1 Such a rhythm, called complete heart block, usually becomes established at ventricular rates of 35 or below most commonly at about 30

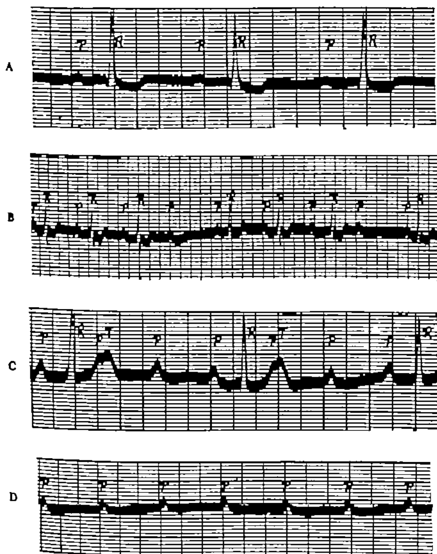


FIG. 164 Electrocardiograms (Lead 2) of partial atrioventricular block (*A*) simple delay in conduction (*P-R* interval = 0.32 second) (*B*) occasional dropped beats, with varying *P-R* intervals giving rise to the "Wenckebach periods at the time of the dropped beats (unequal to the interval covering two usual beats) (*C*) three to one block; and (*D*) entire absence of ventricular contractions during Morgagni-Adams-Stokes attack. Time interval = 0.2 second.

per minute, but higher in infants and young children, for example, at about 50 per minute. Two to one atrioventricular block with an atrial rate at the normal average of 72 gives a ventricular rate of 36, which is but slightly higher than the usual rate in complete heart block. These observations are important for they help to explain the occasional transitions back and forth between partial heart block and so-called complete heart block, which transitions have been sometimes regarded as mysterious. Also they explain the rarity of long ventricular standstill and of the Morgagni Adams-Stokes syndrome. The atrioventricular nodal pacemaker usually escapes to prevent this syndrome; rarely is it unable to do so because it is itself depressed. Finally the observations noted above explain the occasional instances in supposedly complete heart block when an atrial impulse passes through the junction to give rise to a ventricular contraction. In other words, "complete heart block" does not mean that impulses can never pass from atria to ventricles.

Rarely a state of double atrioventricular block exists in which there is not only complete dissociation between atria and ventricles but the idioventricular pacemaker itself may be blocked, as in an early patient of my own whose electrocardiogram showed complete atrioventricular block and partial (2 to 1) idioventricular block (White, 1918) and in a recent case of Langendorf and Katz (1942)

The ventricular rhythm in heart block of atrioventricular type may be regular or irregular Usually it is regular due to the fact that there is simply a uniform delay in conduction time without dropped beats, a regular 2 to 1 3 to 1 or complete block sequence also produces regular ventricular action but at slow rates of 40 to 20 When the ventricular action is irregular it is regularly irregular for a dominant rhythm is maintained and in the arterial pulse equal spacing" of large groups of beats against each other is possible but equal spacing may not be found if comparison of the arrhythmia with the regular beats is limited to the pause due to the dropping of a beat, since the interval between the beats preceding and following a dropped beat may or may not be equal to the length of two normal cycles It frequently is shorter because of the progressive delay that may occur in conduction (increasing *P-R* intervals) up to the time of the dropped beat with marked shortening of the *P-R* interval of the first beat after the pause, due to recovery of the conducting tissue (Figure 164B page 935) This variation in conduction not only causes the pause in the arteriogram to be considerably shorter than the interval covered by two other cycles but it also results in some inequality in length of the normal cycles (the pauses in heart block with dropped beats have sometimes been called "Wenckebach's periods)

The atrial rate in a-v block is usually regular but there may be any kind of atrial arrhythmia with any grade of block. An interesting form of atrial arrhythmia is occasionally found in complete heart block and consists of a temporary quickening of the s-a rhythm or prematurity of normal atrial complexes in the electrocardiogram when they fall directly after the ventricular contractions, quite possibly due to the stimulus to the s-a node by the

vigorous ventricular contraction. Sometimes also, even in complete a v block, retrograde atrial contractions occur Atrial fibrillation is a not very rare accompaniment of complete heart block, and atrial flutter has also been noted.

Etiology *Cause* Atrioventricular block is caused either by temporary toxic or functional conditions, by permanent organic disease, or by both factors acting together It is most commonly temporary and functional but this type is likely to be missed, because it is so transient and usually so slight in degree. Examples of temporary or functional causes of atrioventricular block are asphyxia, excessive vagal stimulation, digitalis poisoning, quinidine poisoning, the effect of other vegetable or mineral poisons, uremia, and the temporary effects of certain infectious diseases such as rheumatic fever and diphtheria, from which recovery may take place without persistence of heart block.

Permanent and organic block is the result most frequently of extensive coronary disease. There may be at first simply a narrowing of the vessel or vessels supplying the junctional tissues with blood, with temporary or slight atrioventricular block which varies with the activity of the subject and with the state of the circulation. With greater narrowing of the coronary vessels and limitation of blood supply the block becomes more permanent and greater in degree, although the junctional tissue itself may show astonishingly little pathologic change. Finally with great or complete arterial occlusion and obstruction to the blood supply the block may become complete and there may or may not prove to be extensive or complete degeneration and fibrosis of the atrioventricular bundle and node (actually a small infarct) An interesting occasional cause of paroxysmal a-v block lasting for a few hours or a few days, accompanying infarction of the posterior wall of the left ventricle, is acute occlusion by thrombosis of the right coronary artery or of the circumflex branch of the left, whence is derived the major part of the blood supply to the a-v junctional tissues in almost all individuals. Other less commonly acquired, but important, causes of permanent and organic block are virus diseases like epidemic parotitis (mumps) which have been more often recognized as factors in recent years, syphilis acting directly by infection of the bundle of His or more often by pressure from adjacent gummata, destructive lesions following diphtheria in rare cases, the results of rheumatic inflammation, invasion of the junctional tissue by the vegetative lesions of bacterial endocarditis, and very rare causes like pressure from neoplasms and cysts, miliary tuberculosis, and trauma. Finally atrioventricular block may be of congenital origin in rare cases, associated with interventricular septal defects and abnormal course or development of the junctional tissues congenital block may be partial or complete.

Sex. The male sex shows permanent heart block twice as often as does the female, probably because of the higher incidence of serious coronary disease in males, but both sexes are about equally affected by temporary or functional block.

Age Atrioventricular block is much more common in older persons because of their greater incidence of serious coronary disease. About 90 per cent of

the higher grades of permanent heart block occur after the age of fifty years.

Pathology No lesion at all may be found in the junctional tissues when there is transient or functional atrioventricular block rarely there may be no obvious lesion even with more or less permanent block of high grade. On the other hand, there may be considerable inflammation, degeneration, or fibrosis of the atrioventricular bundle and node without heart block. Thus, there is by no means a close correlation between the degree of atrioventricular block and the condition of the atrioventricular junctional tissues partly because of the fact that heart block is essentially a functional disturbance not necessarily dependent on obvious disease, partly because the damage may be more in the coronary vessel or vessels supplying the node and bundle than in the node and bundle themselves and these vessels are not always carefully studied, and partly because a small amount of tissue may be able to carry on normal function in spite of much damage or destruction of the bundle as a whole. It is true, however that permanent atrioventricular block of high degree is usually associated with extensive pathologic changes in the junctional tissue (inflammation degeneration or fibrosis) It is important in the postmortem study of the heart of a patient with atrioventricular block to examine the coronary vessels supplying the junctional tissues for narrowing or occlusion, as well as to study the conducting tissues itself.

Fibrosis of the bundle of His from coronary arteriosclerosis is the lesion most commonly found in heart block, infiltration by rheumatic, syphilitic, or other infectious process, like bacterial endocarditis, and calcareous extension from the region of mitral or aortic valve, which is calcified at its base, is occasionally encountered, while congenital defects of the bundle are rare. As time passes we have become aware that now and then infectious diseases of childhood and youth may result in scarring of the junctional tissue which, quite symptomless, may be wrongly ascribed to congenital or coronary etiology

It is of more than passing interest that atrioventricular block is an uncommon complication of massive coronary thrombosis with myocardial infarction diagnosable clinically while relatively few cases of atrioventricular block have had a history of acute clinical myocardial infarction. The answer lies in the fact that occlusion of some of the larger coronary vessels may occur with serious heart damage but escape of the particular part of the heart in which lie the node of Tawara and bundle of His, while a localized occlusion of the small vessels supplying these specialized structures creates too slight a clinical disturbance to be recognized in most cases the seriousness of the two conditions as evidence of important coronary heart disease is, however much the same. Of a series of 328 cases of "clinical" myocardial infarction analyzed only 3 6 per cent had atrioventricular block, while of 117 patients with atrioventricular block only 11 9 per cent had had a history of myocardial infarction; the frequency of angina pectoris was even less, there having been but 1 5 per cent of cases of atrioventricular block among 700 patients with angina pectoris without "clinical myocardial infarction and 9 4 per cent of cases of

angina pectoris without myocardial infarction among the 117 patients with atrioventricular block (Salcedo and White, 1935)

Symptoms. Atrioventricular block rarely causes any symptoms, since it is usually of slight degree· even block of high degree with dropped beats or very slow pulse may remain unnoticed by the patient. Sometimes, however there is complaint of a disagreeable palpitation, due either to the pause in the heart's action when the atrial impulse is blocked, to the forceful thump following the pause, or to the constant pounding when the heart beats very slowly (about 30 per minute) The sensitiveness of the patient rather than the irregularity or slowness of the pulse determines the presence or absence of symptoms. Pain and dyspnea are not common they are the result of complicating angina pectoris, congestive heart failure, or neurocirculatory asthenia.

Much has been written in the past about the *Morgagni Adams Stokes* syndrome, perhaps too much in view of its rarity Nevertheless, it is an important complication of atrioventricular block when it does appear This syndrome as originally described, consists in the association of syncope and epileptiform convulsions with marked slowing of the heart s action (Morgagni, 1760· Adams, 1827 Stokes, 1846) but all grades of disturbance of the cerebral circulation may exist from slight dizziness and faintness with transient ventricular standstill of two or three seconds duration up to extreme degrees of the syndrome with cessation of the heartbeat for as long as twenty or thirty seconds (Figure 164D page 935) The patient with these distressing symptoms may have warning and find time to sit or to lie down, or he may fall to the ground suddenly while standing or walking. The clinical condition is similar to the result of the cerebral anemia occurring in some cases of extreme tachycardia or of atrial depression with standstill of atria as well as ventricles, but the mechanism is of course quite different and the prognosis and treatment not the same. It is better not to lump all these conditions into this one heading as has been somewhat the custom. An electrocardiogram should be secured between attacks to see whether or not some degree of atrioventricular block is present. As a rule sudden ventricular standstill due to atrioventricular block does not happen without at least some delay in conduction at other times, rarely paroxysmal atrioventricular block does occur but graphic records are necessary for its proof.

Signs. The pathognomonic sign of atrioventricular block is either (1) delay in the interval between the atrial and the ventricular pressure waves in the venous pulse (*a-c* interval) beyond the normal, usually put at 0.2 second, or between the atrial and the ventricular electric waves in the electrocardiogram (*P-R* interval) beyond the normal, the upper limit of which is routinely placed at 0.2 second, and with or without "dropped beats (rare to many) (Figure 164 page 935) or (2) complete dissociation between atrial and ventricular rhythms with slow ventricular rate.

A *P R* interval of 0.2 second is traditionally the upper limit of normal, but such a measurement must be analyzed with care in every case. The range of normal is wide in this particular as in many others (see Chapter 2) In infants

the normal varies from 0.08 to 0.14 second, in children from 0.10 to 0.18 second, and in adults from 0.12 to 0.22 second. Thus 0.20 second would be well within the normal for one adult and prolonged for another whose average should be perhaps 0.15 second. One must use considerable judgment and sometimes secure serial records over long intervals of time for sure appraisal of variations of atrioventricular conduction time unless they are grossly abnormal.

With training and experience it is often possible to analyze the jugular venous pulse by inspection and to observe well-marked delay in the interval between atrial and ventricular waves, or to see completely blocked atrial waves falling in longer ventricular pauses. The difficulty or impossibility of noting slight changes, however, and the likelihood of confusion even after training, make graphic records—preferably electrocardiograms—essential for the establishment of the diagnosis of atrioventricular block in all but the most marked cases in which there happen to be actual dropped beats or very slow pulse rates (35 or less per minute). The phlebogram by measurement and the electrocardiogram at a glance show the presence and grade of block (Figures 36, page 167, and 164, page 935). Mechanical pulse tracings taken from cardiac apex or arm artery may rarely show the atrial pressure waves and the presence of block (Figure 31, page 158), but the chief value of the analysis of the ventricular action in arteriogram or cardiogram in heart block is in the finding of a dominant rhythm when there are dropped beats. Without auscultation, however, this finding does not tell whether the pause is due to a true dropped beat or to a ventricular premature beat that has failed to show itself in the arterial pulse. Moreover, the varying conduction time that often occurs before and after a dropped beat shortens the pause and may be confusing in measurements of the arteriogram.

Auscultation in atrioventricular block may sometimes reveal an extra sound, usually faintly heard and often double, due to the atrial contraction, which may be separated sufficiently from the ventricular contraction to be clearly heard in a few cases. This additional sound may come just before the normal first heart sound, making the latter seem reduplicated, or it may come well before it, and, if the heart rate is fast, give rise to a presystolic gallop rhythm. If there is considerable delay in conduction, the extra sound may come in the middle of diastole, early in diastole, or immediately after the normal second heart sound, giving rise respectively, if the heart action is fast, to middiastolic gallop rhythm, protodiastolic gallop rhythm, or simple reduplication of the second sound (Chapter 5). Finally, in heart block of high degree, with dropped beats, or in complete atrioventricular block, the atrial contractions may be heard, usually dimly, at regular intervals between the ventricular contractions, or they may at times coincide with the ventricular contractions causing an accentuation of the first, second, or third sound (Figures 13 and 14 in Chapter 5).

The heart rate in atrioventricular block is as a rule normal, because there are generally no dropped beats and the atrial rate is unaffected. With dropped

beats, showing a higher grade of block, the ventricular and peripheral pulse rates fall and tend at first to be irregular With 2 to 1 and complete heart block the heart rate falls to 40 30 and rarely somewhat lower Very marked slowing of the pulse down to 20 10, or even 2 or 3 beats a minute is rare and always very transient It is due to depression of the idioventricular pacemaker which does not take up the control of the heart when the atrial impulses are almost completely blocked off from the ventricles, or else it is due to this same ventricular pacemaker depression coming on periodically in the course of complete heart block. It is most common in the transitional stage between partial atrioventricular block of high grade and complete block before the idioventricular rhythm has become established. When complete heart block is well established, excessive slowing of the beartbeat, though possible, is rare. It is the ventricular standstill with cerebral anemia occurring with this extreme slowing of the heart rate that is responsible for the syncopal attacks in the Morgagni-Adams-Stokes syndrome. The slowest heart rate that has been recorded is one beat a minute (Odriozola, 1920) but ventricular standstill of from 2 to 3 minutes, with recovery has been reported also of course this must necessarily be a transient condition If it is more prolonged or often repeated, death results. The longest period of ventricular standstill proved electrocardiographically has been, so far as I know 79 seconds, following a period of over 3 minutes of abnormal ventricular tachycardia, including ventricular fibrillation; in this patient no pulse or cardiac contraction could be seen, felt, or heard for a period of 5 minutes recovery with two months more of life followed an injection of epinephrine directly into the heart (Levine and Matton, 1926) The more recent notable case of a twenty-minute cardiac arrest, with complete recovery after cardiac massage, apparently involved the whole heart (Adams and Hand, 1942)

The reaction of the heart rate to various factors in the presence of atrioventricular block is of interest. Often with lesser grades it increases normally with exercise and excitement, but often, even with lesser grades, the reverse happens and the heart slows. This paradoxical condition is due to the increase in the grade of block and number of dropped beats as a result of the increase in atrial rate the conducting tissue is no longer able to carry every impulse at the increased atrial rate so that 2 to 1 block develops with marked slowing of the ventricular rate while there is simply delayed conduction at only a moderately slow heart rate. For example, at rest both atrial and ventricular rates may be the same, 72 per minute, while on exercise the atrial rate may rise to 96, and the ventricular rate fall to 48 (2 to 1 block) The variation in atrial rate dependent on respiration may also in a critical case have a similar effect (Bourne, 1928) this is particularly true in the case of Cheyne Stokes respiration. Vagal stimulation by carotid sinus pressure and also the administration of digitalis may easily convert a slight grade of atrioventricular block into a high grade, though rarely if ever complete.

The blood pressure is unaffected in heart block unless the ventricular rate is very slow (about 30 per minute) when there tends to be a rather high

systolic pressure (150 to 160 mm) and a full pulse pressure (from 80 to 100 mm) this is a more or less compensatory condition and is due to increased filling of the heart during the prolonged diastole together with full emptying during the prolonged systole that always accompanies a slow pulse rate. Considerable hypertension however in a case with complete heart block is always a complication and never a part of the circulatory mechanism of complete heart block itself

The blood flow at rest in atrioventricular block is not remarkable, even at very slow heart rates, because with a slow pulse the output of the heart per beat is almost correspondingly increased. An output of 120 cc of blood per beat at a heart rate of 35 per minute gives a minute volume of blood flow of 4 2 liters, not much less than that of the normal 4 9 liters at a heart rate of 70 and an output of 70 cc per beat. With complete heart block, however and to a less extent with partial block of high degree, there is relatively little variation of the blood flow possible with exercise, on account of the inability of the heart to increase its rate and because the ventricles are already putting out almost their maximum capacity per beat.

Roentgen ray studies are of little or no help in the analysis of atrioventricular block although it is frequently possible to observe fluoroscopically the independent atrial and ventricular actions, and, when the ventricular rate is very slow to note the increased fullness of cardiac contraction with enlargement which may be entirely due to the increased diastolic filling.

Electrocardiography is the only satisfactory method for the analysis of this disturbance of rhythm (Figure 164 page 935) it has also the great advantage of giving other evidence especially *T* wave changes, of any very extensive or rapidly progressive coronary heart disease.

There may or may not be signs of cardiac enlargement and failure, valvular disease, and hypertension. Usually there are cardiac signs of some sort, especially enlargement, with the greater degrees of atrioventricular block.

Course and prognosis. Atrioventricular block is always important, not so often in itself as in showing the existence of serious disease or toxic states. This disturbance of rhythm is usually an incidental or accidental discovery in the course of routine health examinations or during the study of some illness, cardiac or noncardiac. It is discovered only very rarely at the time of its origin. The only sign of its presence may be electrocardiographic, or there may be the extreme signs and symptoms of block of high degree with the Morgagni-Adams-Stokes syndrome.

In young persons not acutely ill with rheumatic or other infection the finding of atrioventricular block, even of highest grades, is compatible with good health and full activity for many years and even for long lives, this seems to be particularly true of instances of congenital heart block that survive early childhood. Even pregnancy has been normally carried through in cases of complete heart block with good reserve and little or no other evidence of heart disease In older persons new heart block is more serious, even in slight grades, unless digitalis is responsible, for coronary disease of progressive character is

likely to be the cause and sometimes angina pectoris is associated with it. When the heart block appears in the course of an acute infection at any age it adds somewhat to the gravity of the prognosis for it may mean serious cardiac involvement. Rarely atrioventricular block may itself kill as the result of ventricular standstill. Such a fate is usually ushered in by attacks of syncope, the Morgagni-Adams-Stokes syndrome, but this syndrome does not always end fatally: it may occasionally be a temporary condition with complete recovery following the establishment of a stable complete heart block or very uncommonly a return to normal rhythm to be followed by normal activity and years of life.

Complications. The only important complications of atrioventricular block are gross myocardial infarction, angina pectoris, congestive heart failure, the Morgagni-Adams-Stokes syndrome, and intraventricular block, the last named will be discussed later in the present chapter. Congenital interventricular septal defects are the rule in the very rare cases of congenital heart block.

Treatment. Atrioventricular block rarely needs any treatment for itself but it frequently is associated with or due to some disease which does demand treatment, especially rheumatic infection, syphilis, and coronary heart disease with myocardial infarction or angina pectoris. Improvement of these conditions, spontaneously or with the help of more or less specific therapy may be attended by a decrease or disappearance of the heart block. A few striking cases of lessening of heart block in syphilis following specific therapy have been reported, probably due to the cleaning up of a gumma pressing on the atrioventricular junctional tissue or of an inflammatory condition of the tissues themselves. Full salicylate therapy has been said to have reduced acute rheumatic heart block, and the new hormone therapy with ACTH or cortisone is very encouraging (see Chapter 14). Rest and other treatment of angina pectoris have at times been followed by decrease in coincident heart block. The high-grade heart block that may appear paroxysmally for a few hours or a few days at the onset of myocardial infarction, usually of the posterior wall of the left ventricle secondary to acute occlusion of the right coronary artery or of the circumflex branch of the left, tends to clear up spontaneously without special therapy other than complete rest, but its amelioration can be effected on occasion by the use of the nitrites, especially erythrol tetranitrate 0.015 to 0.03 gm (¼ to ½ gr) every three or four hours. Ample antitoxin therapy of severe diphtheria has been associated with recovery after the appearance of atrioventricular block. Finally, the treatment of congestive failure by digitalis in some cases complicated by atrioventricular block has even resulted in the reduction of the grade of block along with general improvement, in spite of the fact that digitalis itself is sometimes alone responsible for heart block.

If certain toxic agents like quinidine and digitalis are the cause of a serious grade of heart block they should be at once omitted; if they produce but slight grades of block they may be discontinued or else reduced in amount, careful watch being established that the block be not increased.

In the presence of atrioventricular block not produced by some poison that

can be controlled, some attention to the future health of the affected individu should be given, even though there be no symptoms produced by the block o any evident heart disease Care should be exercised to avoid extreme fatigue overexertion, and infections, but otherwise there should be no restrictions o therapy unless particularly indicated. The finding of heart block, especiall in a young person, needs in no way to render him a cripple, but electrocardi ograms and physical examination at intervals, perhaps once every year or two, are useful guides to the progress, favorable or unfavorable, of the state of the heart.

Finally in rare instances it is necessary to treat the heart block itself, when ventricular standstill is so frequent or of such long duration that cerebral symptoms develop dizziness, faintness, syncope, and convulsions (Morgagni-Adams-Stokes syndrome) The most that can be done as a rule is to give therapy to prevent the attacks rarely an attack itself can be treated if it is of long duration and facilities are at hand. The most effective measure in the prevention of the Morgagni Adams-Stokes syndrome is the subcutaneous or intramuscular injection of *epinephrine (adrenaline) hydrochloride* 0.25 to 1 cc of the 1 1 000 solution (equaling 0.25 to 1 mg) at intervals of every few hours as needed (introduced by Hardoy and Houssay 1917 and by Phear and Parkinson, 1922) Recently epinephrine in oil (2 mg of epinephrine hydrochloride in 1 cc of sesame or peanut oil) has been introduced in this prophylactic therapy with the advantage that because of its slow absorption under the skin only one or two injections may be needed in 24 hours, when the effect is beginning to wear off massage of the site of injection will introduce some of the as yet unabsorbed epinephrine into the circulation. This is almost invariably effective in preventing ventricular standstill either by decreasing the grade of atrioventricular block or more commonly by stimulating the activity of the idioventricular pacemaker The heart rate may be maintained above 30 per minute, sometimes even as high as 50 for hours or days at a time by this therapy The atrial rate is simultaneously raised by the epinephrine to 90 or 100 or more Less effective immediately but more gradual and prolonged in its action, and closely related in effect to epinephrine, is *ephedrine* given in the dose of 15 to 30 mg (¼ to ½ gr) of the hydrochloride three to six times daily by mouth sometimes considerable nervousness results from its use Paredrine, a similar drug, has also been used with favorable effect, given in the dosage of 40 to 60 mg by mouth three times a day (Nathanson, et al., 1942) Very rarely even digitalis may be tried if it keeps the a-a rate from rising to critical levels above which serious a-v block is set off. Finally three other drugs have been given thyroid extract or thyroxin, barium chloride, and atropine sulfate. Each of these drugs has sometimes succeeded but more often failed they are less effective than epinephrine and ephedrine and rarely worth bothering about.

For emergency treatment of a prolonged period of ventricular standstill, with syncope, convulsions, and apparently impending death, the intracardiac injection (by long needle) of 0 1 to 0.5 cc of 0 1 per cent solution of epi-

nephrine hydrochloride (i.e. 1 1 000) may be tried (though usually unsuccessfully) provided ventricular fibrillation is not itself the cause of the asystole; electrocardiographic evidence of previous attacks of the Morgagni Adams-Stokes syndrome in the case in question is important. Epinephrine may be lifesaving if administered within a few minutes of the cessation of the heartbeat, but the drug is not without danger since it can itself induce ventricular tachycardia and fibrillation (Hoff and Nahum, 1934) large dosage, such as a full cc of 1 1000 epinephrine hydrochloride solution should for that reason be avoided.

Differential diagnosis. Atrioventricular block, when there is simply delayed conduction, can be differentiated with certainty from normal rhythm only by the electrocardiogram or by a good phlebogram. When there are dropped beats, heart block is to be differentiated from premature beats which are very early or very faint careful auscultation usually permits a clear distinction between the two. Finally atrioventricular block of high degree must be distinguished from marked sinoatrial bradycardia or block, which usually requires venous or electric tracings for diagnosis but which can at times be detected by trained observation of the jugular pulse. The Morgagni-Adams-Stokes syndrome is to be differentiated from other cause of syncope and convulsions, usually an easy matter because of the very slow heart rate or actual cardiac standstill, the absence of paralysis, the absence of a previous history of epilepsy nephritis, diabetes, and neurocirculatory asthenia, and the presence of other signs of heart disease besides the block itself. It is, however important to note that high-grade heart block may be wholly paroxysmal with normal *P-R* interval between the relatively short periods of bradycardia or syncope. Electrocardiograms or at least direct observation of the heart rate should always be secured during the actual attacks.

INTRAVENTRICULAR (BUNDLE BRANCH) BLOCK

When there is depression of conduction in the branches of the atrioventricular bundle, intraventricular or bundle branch block is said to exist. Undoubtedly much of this intraventricular block is unrecognizable, because either it is slight in degree in the larger branches or it affects only a limited number of the smaller branches of the conducting system (Purkinje network-Purkinje, 1845) When block exists to a moderate or marked degree in either of the two main bundle branches (right or left) or in a very extensive area of the finer network, it becomes evident in the electrocardiogram, but its presence cannot be proved in any other way It is better to speak of lesser grades of intraventricular block of left bundle branch type, or of right bundle branch type or of uncertain type (slight aberration) than to use the term arborization block, for it is as yet impossible to distinguish partial bundle branch block of either main branch from extensive block of the lesser branches.

Incidence. As is the case with slight grades of atrioventricular block, intraventricular block is undoubtedly more frequent than statistics generally indi

cate, since electrocardiograms are essential for its detection. Intraventricular block of all grades is somewhat more common than atrioventricular block of all grades. Of 10 000 cases electrocardiographed at the Massachusetts General Hospital during the fifteen years from 1916 to 1930 inclusive there were 734 cases of intraventricular block (7 3 per cent) and 641 cases of atrioventricular block (6 4 per cent) Of the cases of intraventricular block 223 showed full degrees, or marked preponderance, of left or of right bundle branch block, and 511 lesser grades of block the left bundle branch type was considerably more common than the right but not to the extent it was once thought to be before the introduction of the precordial leads or the recognition that a wide *S* wave in Lead 1 usually indicates a type or grade of right bundle branch block. During the decade from 1934 to 1943 inclusive there were at the Massachusetts General Hospital 1 040 cases of clear-cut bundle branch block of either branch type, 258 of which were right and 782 left.

Mechanism (abnormal physiology). Bundle branch block may be due, as in the case of atrioventricular block, either to temporary functional or to permanent organic conditions, but temporary or functional bundle branch block is very rare compared to both permanent bundle branch block and functional or temporary atrioventricular block. Conduction when depressed in both main bundle branches equally may give rise to a condition that is indistinguishable from atrioventricular block, but when one branch is more depressed than the other or some very extensive area of the finer arborizations is affected, the lack of balance is shown in the electrocardiogram which simulates a dextrogram or a levogram. If the left bundle branch is diseased or depressed so that the impulse is delayed in reaching the left ventricle, spreading to the ventricular muscle wholly or in large part by the right branch, the condition is called left bundle branch block and the electrocardiogram has the character of a dextrogram (Figure 165) when the right bundle branch conduction is grossly defective, the ventricular deflections of the electrocardiogram resemble the levogram and right bundle branch block is present (Figure 166) The nomenclature is that based on the convincing work and conclusions of Mann and of Wilson and his associates and of others in recent years, in opposition to the older point of view now largely discarded with its opposite nomenclature of bundle branch block.

Wilson (1942) called attention to the reason for the earlier confusion based on the common dissimilarity of the curves of bundle branch block in man and in the dog. The crux of the situation lies in the universally median "vertical" position of the dog s heart in contrast to the commonly diagonal or horizontal position of man s heart. As Wilson says, had direct or precordial leads been taken earlier the confusion need never have arisen.

Between the two extreme conditions of full left and full right bundle branch block there are various grades and combinations of intraventricular block sometimes difficult accurately to analyze. Intraventricular block is frequently found present when there are high degrees of atrioventricular block.

The criterion for the diagnosis of bundle branch block is an abnormal

width or duration of the first ventricular complex, that is, the *QRS* wave, provided the *P-R* interval is not too short (that is, not so little as 0 1 second or less) An upper limit of 0.1 second has been more or less routinely regarded as the borderline beyond which bundle branch block is to be diagnosed, but it is undoubtedly true that on occasion the normal may exceed that slightly

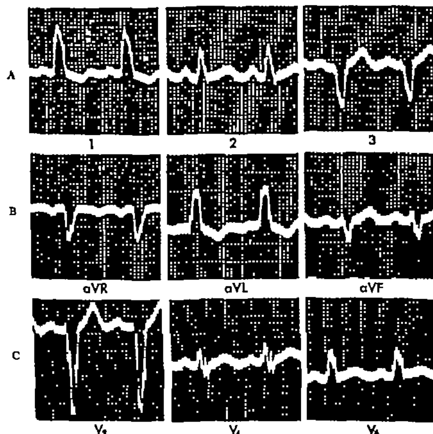


FIG. 165 Electrocardiogram in left bundle branch block, female, age 68. (*A*) Bipolar limb leads 1 2, and 3 (*B*) unipolar limb leads, VR, VL, and VF (*C*) three precordial leads, V V and V. Note the wide *QRS* waves throughout, the left axis deviation in the limb leads, and especially the notched and slurred *R* waves in Leads V and V Time = 0 04 and 0.20 second, amplitude 1 mm = 0.10 mv

(up to 0 11 second or even a shade more) and also that very large hearts (dilated, hypertrophied, or both) can have widened *QRS* waves (up to 0 12 second) without actual bundle branch block. It is of some related interest that the very large heart of the normal elephant has a wide *QRS* wave of about 0 2 second and that the human infant's heart records a *QRS* wave of only 0 05 second Thus, as in the case of the *P R* interval, so too in judgment concerning the *QRS* wave much care must be used, with full recognition of the

wide range of the normal heart (see Chapter 2) the electrocardiographic time intervals are to a certain extent at least, a function of heart size.

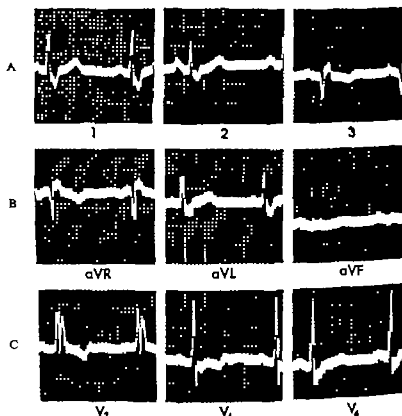


FIG. 166. Electrocardiogram in right bundle branch block, male, age 60. (*A*) Bipolar limb leads 1 2, and 3 (*B*) unipolar limb leads, aVR, VL, and aVF (*C*) three precordial leads, V V and V Note the wide *Q* waves in Leads 1 2, VL, and V the wide *R* waves in Leads 3 and VR, and especially the wide M-shaped *R* waves in Lead V Time = 0 04 and 0.20 second, amplitude 1 mm = 0.10 m

There may occur as in the case of most other disturbances of rhythm and conduction paroxysmal bundle branch block, such a mechanism which may antedate by weeks or months a permanent change. An interesting variation is 2 to 1 bundle branch block (see Figure 167)

Etiology *Cause* The commonest cause of bundle branch block is coronary atherosclerosis, resulting in faulty nutrition, degeneration, and eventual fibrosis of the larger or smaller bundle branches. Occlusion of a large coronary artery (more often the right or the circumflex branch of the left) or of the smaller vessels which supply the bundle branches may be followed by infarction involving right or left main trunks or lesser branches.

There is a considerable discrepancy however between the occurrence of bundle branch block and the clinical evidence of coronary heart disease, although less than in the case of atrioventricular block. In a series of 700 pa-

tients with angina pectoris without "myocardial infarction there were 7 7 per cent who showed intraventricular block (as compared to 1 5 per cent who showed atrioventricular block) while among 328 cases of myocardial in-

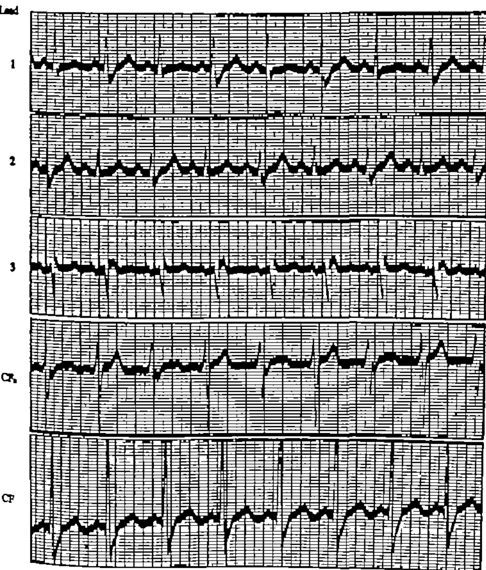


FIG. 167 Alternating right bundle branch block in man, age 59 The alternation has cleared in Lead CF in which lead there is constant right bundle branch block. Time = 0.10 and 0.20 second, amplitude 1 mm = 0.10 m

farction there were 9.5 per cent with intraventricular block (4 2 per cent had atrioventricular block) on the other hand, among 181 cases of bundle branch block of all grades, 39 1 per cent showed angina pectoris without myo-

cardial infarction (29 8 per cent) or myocardial infarction with or without angina pectoris (9 3 per cent) (Salcedo and White, 1935)

Other less common causes of organic intraventricular block are scarring from rheumatic myocarditis (preponderantly involving the right bundle branch) syphilitic infection in the heart (gummatous or diffuse) acute diphtheria (when it is especially serious and likely to be fatal) rarely other infections such as from viruses or bacterial endocarditis, and very rarely tumors and trauma.

Of a series of 52 cases of intraventricular block, 44 or 84 6 per cent were thought to be due to coronary disease, 3 cases (5 8 per cent) were apparently rheumatic, 3 cases were syphilitic, and 2 cases were of unknown cause (White and Jones, 1928)

Functional intraventricular block, transient in occurrence, is relatively infrequent. It has, however been noted as a toxic result of too much digitalis or quinidine or of other poisoning. It may occur as the result of fatigue in very rapid heart action, as temporarily in atrial flutter without atrioventricular block.

Sex. Males show bundle branch block much more commonly than do females, probably because of a higher incidence of serious coronary disease. The ratio is about 3 to 1

Age Bundle branch block is much more common in older persons, 80 per cent of the cases being more than 50 years old. It is very rare in infancy and early childhood.

Pathology In a few cases of established intraventricular block no pathologic change is found in the bundle branches, but it is probable that in most of these exceptions there is a limited blood supply because of coronary disease In instances in which some temporary poison, fatigue from tachycardia, or unusual vagus stimulation is responsible, naturally no pathologic change is to be expected functional and organic factors may however be combined. It is usual to find some changes, especially fibrosis in the bundle branches in pronounced degrees of intraventricular block, but the search in the human heart is a difficult one, and much experience and patience are required for identification of the bundle branches and their careful study as yet there is insufficient information about their structural pathology A source of confusion is that both bundle branches may show considerable pathologic change when the electrocardiogram indicates either left or right branch block, or there may even be more change on the opposite side (Yater 1938) the explanation is probably that the structural changes alone are inadequate to account for the whole picture and that a few conducting fibers on one side may be more effective than a large number on the other side for some reason, perhaps because of a difference in blood supply It is apparently rare for bundle branch damage or depression to be wholly unilateral.

Symptoms. There are no symptoms of bundle branch block. There are frequently associated, however the symptoms of angina pectoris and congestive failure, and palpitation due to various complicating arrhythmias.

Signs. There are no characteristic signs of bundle branch block except the pathognomonic electrocardiograms on which the diagnosis depends (Figures 165 page 947 and 166, page 948) There may be in some cases reduplication of one or of both heart sounds due to the somewhat asynchronous contractions of the ventricles resulting from bundle branch block, but this sign is not constant. When both heart sounds are clearly reduplicated, intraventricular block should be looked for

Usually heart disease is evident when there is bundle branch block. Cardiac enlargement is a common finding but valvular disease is relatively infrequent. Hypertension occasionally exists, and there may be signs of heart failure. Roentgen ray examination is of no particular help

Course and prognosis. Bundle branch block of slight degree may be a relatively unimportant accidental discovery or it may be associated with serious and rapidly fatal heart disease, such as extensive infarction from coronary thrombosis. In some cases it exists unchanged for many years, allowing full activity but in others it may change in the course of weeks or months, increasing in degree along with symptoms and signs of progressive heart failure. It may be entirely unimportant in rare cases, occurring as a more or less transient effect of vagal stimulation or of fatigue in excessive tachycardia. Of itself it is not fatal, but each case must be analyzed carefully Although the prognosis is to be based largely on other evidence of heart disease, the finding of true bundle branch block of high degree renders the prognosis necessarily more guarded. The average survival time for 281 cases of right bundle branch block was 3 9 years and for 555 cases of left bundle branch block 3 3 years (see below) The 185 cases of right bundle branch block who survived the first year of follow-up had an average survival time of 5 7 years, and the 356 cases of left bundle branch block who survived the first year had an average survival time of 4 9 years. From these figures it would appear that the right bundle branch block may show a slightly better prognosis than left bundle branch block, however an analysis of the survival time at different age groups indicates that after the age of 50 there is only slight difference between the average survival periods of right and left bundle branch block either in the total number of patients or in the group who survived the first year

There seem to be two general clinical groups of cases with bundle branch block, (1) that with a rapidly bad prognosis based largely on the presence of evidence of extensive heart disease, usually considerable enlargement and some degree of myocardial or coronary insufficiency and (2) that with a good prognosis of years of life and activity in which the bundle branch block is the only abnormal finding· despite this general trend, accurate prognosis in an individual case is often difficult. It is the general finding at present that the cases with the lesser grades of right bundle branch block (wide *S* waves in Lead 1) survive the longest; statistics are accumulating but are not yet fully adequate.

Among others three series of cases of bundle branch block have been considered prognostically in recent years. One series of 126 patients showed a high

mortality during the first year (60 cases, nearly 50 per cent) 15 of the cases died during the next few years, and 11 were still living 4 to 8 years after the discovery of the lesion neither the configuration of the electrocardiogram nor the duration of the *QRS* deflection seemed to be of prognostic significance (Kaplan and Katz, 1939) On the other hand, a series of cases reported by Perera, Levine and Erlanger (1942) showed a considerably longer average survival time for right bundle branch block (3 years for 29 fatal cases) than for left (1 year and 2 months for 60 fatal cases) long-time survivors in each group were still alive, the longest exceeding 17 years for the right and 15 years for the left. A third, more recent, series (Shreenivas, et al., 1950) referred to above, has dealt with larger numbers over a longer interval A series of 281 cases of right bundle branch block electrocardiographed at the Massachusetts General Hospital gave the following statistical findings death within one year in 45 patients (16 per cent of the total series and 24 per cent of those traced) and survival of 72 cases for more than five years after the bundle branch block was discovered (27 per cent of the total series and 40 per cent of those who could be traced) In a consecutive series of 555 patients with left bundle branch block, also electrocardiographed at the Massachusetts General Hospital, a survival period of less than one year was found in 170 (31 per cent of the total series and 32 per cent of those traced) and of more than five years after the bundle branch block was discovered in 121 (21 per cent of the series and 28 per cent of those who could be traced)

Complications. There are no complications directly due to the bundle branch block, unless in very rare cases both bundle branches are completely blocked, with a resulting condition which is indistinguishable from atrioventricular block; of this possible mechanism we have no definite clinical knowledge Conditions frequently complicating intraventricular block are atrioventricular block of all grades, atrial fibrillation angina pectoris, myocardial infarction, congestive heart failure, pulsus alternans, and hypertension.

Treatment. There is no direct treatment of the bundle branch block, but therapy of any cause that may be recognized may not only help the underlying disease or disorder but also very rarely decrease or abolish the intraventricular block this may happen in the case of atrial flutter or paroxysmal tachycardia with functional bundle branch block, and in syphilitic, rheumatic, or diphtheritic affection of the heart. Complications such as congestive heart failure and angina pectoris should be treated without any regard to the presence of the bundle branch block.

Differential diagnosis. Bundle branch block must be differentiated from a normal ventricular mechanism and this can be done only by electrocardiogram electrocardiography also distinguishes the various types of intraventricular block as described above. Even by electrocardiogram however it may be occasionally difficult in the presence of very rapid heart action to distinguish bundle branch block from ventricular paroxysmal tachycardia it may be necessary to wait till the pulse slows before differentiation is clear There is no particular condition pathologic or otherwise, to be differentiated from

intraventricular block, except the anomalous state of the conducting system in which the impulse is transmitted with excessive speed to one ventricle or the other rather than delayed in the contralateral branch in such cases the P-R interval is excessively short and that is the clue that makes the differentiation at once clear (Wolff Parkinson, and White 1930)

WIDE *QRS* WAVE WITH SHORT *P R* INTERVAL

An odd electrocardiographic anomaly (Figure 168) probably congenital in origin, has been found in healthy young persons prone to paroxysmal tachycardia (Wolff, Parkinson and White, 1930) it has the appearance of bundle branch block with short *P-R* interval (0 1 second or less) The wide *QRS* waves may on occasion, spontaneously or after exercise or atropine, sud-

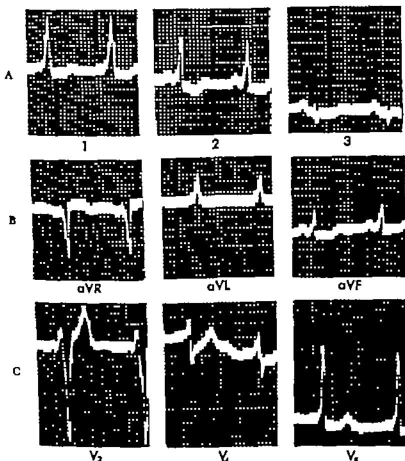


FIG. 168. Electrocardiogram showing short *P R* and wide *QRS* waves (Wolff Parkinson-White syndrome) Male, age 43 (*A*) Bipolar limb leads 1, 2, and 3 (*B*) unipolar limb leads, VR, VL, and VF (*C*) three precordial leads, V V and V Time = 0.04 and 0.20 second, amplitude 1 mm = 0.10 m

denly give way to normal *QRS* waves with normal *P R* intervals. The total duration of the short *P-R* interval plus the wide *QRS* wave is well within normal limits and equal in the same subject to the duration of the normal *P-R* interval plus the normal *QRS* wave to which the case may at times revert. Almost certainly the correct explanation of this anomaly is that there is no bundle branch block at all and that the impulse travels much more rapidly than usual from atrium to one or the other ventricle either (1) by special conducting fibers from sinoatrial node or elsewhere in the atrium to one ventricle or the other (e g. via a bundle of Kent, Kent, 1893) or (2) by supernormal spread down one or the other bundle branch (thus representing a right or left *bundle branch acceleration* instead of the usual reversed left or right bundle branch block) or (3) less likely as the result of two interfering pacemakers, one in the atria and the other in the ventricles (Hunter et al., 1940) thus shortening the *P R* interval and giving rise to a *QRS* wave that in shape resembles that of bundle branch block sometimes the impulse in any given case may pass through the short circuit and sometimes through the usual circuit in the bundle of His.

Almost all the patients have remained in good health but a few have succumbed in middle or in old age to such complications as coronary thrombosis or even apparently to a disturbed heart rhythm (as in a recent case of our own, a woman aged 48 who died suddenly during or after a paroxysm of atrial fibrillation with an excessive heart rate of 300 or slightly more) Autopsies in 2 or 3 cases have apparently revealed an extra bundle (of Kent) (e.g., Öhnell, 1940) The syndrome is not very rare, it makes up about 5 per cent of cases with wide *QRS* waves and about 5 per cent of patients subject to paroxysmal tachycardia (Hunter et al., 1940)

SUDDEN DEATH

The most dramatic disorder of cardiovascular function is that which causes sudden death in fact it was such a source of concern to Pope Clement XI in Rome in the winter of 1705 to 1706 that he directed his physician Lancisi to study the problem by autopsies and otherwise, and in 1707 one of the very few books on the subject was published by Lancisi. Sudden death is apparently due to an abrupt ventricular asystole (from standstill or fibrillation) quite possibly with an additional element of sudden depression of the central nervous system. No adequate reason may be found pathologically for such a death, although there is usually evidence of considerable coronary or aortic disease, consisting generally of marked sclerosis and narrowing of the coronary arteries or of syphilitic aortitis. Sudden death is quite a different matter from the more gradual death from asphyxia in heart failure or from massive pulmonary embolism or from cerebral hemorrhage

Very few cases indeed are explained by cardiac or aortic rupture with abrupt exsanguination. It is most likely that the effective mechanism of the heartbeat itself is suddenly stopped by a great reflex vagal effect with paralysis

of the pacemakers or by the onset of ventricular fibrillation. Already a small group of electrocardiograms taken at the time of death under various conditions has been accumulated but we need many more. With the solution of the mystery there may come progress leading to the resuscitation of some of these victims. Epinephrine and other drugs injected directly into the heart and certain mechanical and electric stimulation such as massage during abdominal operations applied directly after rapid thoracotomy or from under the diaphragm, the prick of a needle with or without electric charge, or even striking the chest wall, have restored the circulation in some individuals whose hearts had stopped beating. Cardiac massage along with the maintenance of artificial respiration has proved the most consistent of the successful procedures to date (Dripps, et al., 1948) Further discussion of cardiac standstill and ventricular fibrillation and possible resuscitation therefrom can be found in Chapter 33 pages 919 to 921 and in this chapter pages 929 930 941 and 944

An important note should be added herewith to this discussion, namely that rations of quinidine sulfate, 3 gr four to six times a day may very possibly prevent the onset of ventricular tachycardia and fibrillation that leads to rapid death in some cases of fresh myocardial infarction or of a high degree of coronary insufficiency as indicated by angina pectoris decubitus (Borg, 1939)

There has been in recent years a revival of interest in the pathologic findings on postmortem examination of persons who had died suddenly I shall summarize four such analyses. Martland (1940) has told of his own experience with the autopsies of 2,000 individuals over the age of ten whose deaths were sudden but not the result of violence: the majority were between 40 and 65 and by far the larger number were males (1 680 or 84 per cent) Organic heart or aortic disease was present in 1,590 (79.5 per cent) 8 per cent had disease of the respiratory organs, 4 per cent of the head, and the remaining 8 5 per cent were subjects with miscellaneous conditions. Of the 1,590 cases of disease of heart or aorta 1 115 (55 per cent of the total 2,000) were of the coronary or hypertensive type, 262 had syphilitic aortitis, 116 rheumatic heart disease, and 97 other types of heart disease. Among the coronary cases which numbered 731 (36.5 per cent of the total) there was coronary occlusion with acute thrombosis in 304 and without acute thrombosis in 314 the remaining 113 cases showing considerable atheroma without actual occlusion of the larger vessels. Well-marked aneurysm of the left ventricle was present in 59 cases and rupture of the ventricular wall in 42 persons. Large hearts without much coronary disease and probably the result of hypertension occurred in 384 cases. Among the 262 syphilitics aneurysm of the aorta was found in 102 cases, aortic regurgitation in 70 and stenosis of the coronary ostia in 80 Rupture of the aorta had occurred in 37 persons of the total series. Aortic stenosis was found in 32 cases, and pulmonary embolism in 10 There was one young colored man who showed at autopsy no abnormalities whatsoever marked apprehension about an impending minor surgical procedure immediately preceded his sudden death, and it was thought that this was an almost

unique example of an overwhelming nervous (vagal) depression of the heartbeat with resulting "death from fright."

Analysis of another group of 123 autopsies in cases of unexplained sudden death (Jeckeln, 1940) showed two thirds to have been the result of heart disease, with coronary lesions forming the great majority six times more often in men than in women. Excessive filling of the stomach with food was frequently found in these fatal "coronary" cases. In 7 cases death was due apparently to syphilitic aortitis, and 5 cases had aortic stenosis, while only 1 had mitral stenosis (with "coronary sclerosis") In 2 cases death resulted from rupture of the aorta and in 3 others from apoplectic cerebral hemorrhage Ruptured aneurysm at the base of the brain (giving rise to a subarachnoid hemorrhage) was found in as many as 19 cases. There were 30 cases of sudden death in children, 6 of which were stillborn, the others being due to a variety of infections, traumatic brain lesions sustained at birth, and acute respiratory disorders.

Lisa (1939) noted the findings in 41 persons dying sudden "cardiac deaths acute coronary thrombosis was present in 10 acute coronary insufficiency was apparently responsible in 5 more, acute endocarditis was found in 5 rheumatic heart disease in 4 syphilis in 8 and pulmonary lesions in 2; 5 cases were infants or children and the remaining 2 were entirely unexplained.

More recently Helpern and Rabson (1945 and 1947) have reported their experience. These authors have analyzed in considerable and interesting detail 2 030 consecutive cases of sudden and unexpected death in the Borough of Manhattan from January 1937 to July 1943 Table 14 below gives the details of this analysis 912 cases or 44 9 per cent involved the heart and aorta, 468 cases or 23 1 per cent involved the respiratory tract, 367 or 17 9 per cent involved the brain and meninges, 198 or 9 7 per cent involved the digestive and genitourinary tracts. There were 90 miscellaneous cases or 4 4 per cent. If we include cases of pulmonary embolism and of cerebral vascular accidents with the cases of heart and aorta to complete the cardiovascular responsibility we have a total of 1 195 cases or 59 0 per cent. The greatest incidence of all these cases was in the decade from 45 to 54 years of age inclusive. Males were preponderant over the females in a ratio of 4 to 1 Among the coronary cases, 80 per cent died instantly Also, among the coronary cases, three fourths showed no grossly fresh thrombosis.

In closing this chapter and the book itself may I suggest that after all neither a high, even 100 per cent, mortality from cardiovascular disease nor sudden death itself are to be regretted, provided they take place at an advanced age after a healthy and happy and useful life right up to the last minute. *In fact* this is actually an ideal goal toward which man may strive, for it means the eradication not only of other diseases, such as the infections of the past, and the cancers, accidents, and the wars of the present, but also the control of the serious cardiovascular threats (such as hypertension and coronary atherosclerosis) to the lives of our youth and middle aged which bid fair to trouble

us for still some years to come. Furthermore we physicians must work hand in hand in our labors with our pioneering colleagues in the gravely needed advances in the social, economic, and spiritual fields of human endeavor. Those of us who have striven during the last generation to probe a little into the depths of our ignorance can turn over with confidence to our successors the far more important task of bringing to pass the aim expressed in the first sentence of this closing paragraph.

Table 14

ANALYSIS OF 2,030 AUTOPSIED CASES OF SUDDEN AND UNEXPECTED NATURAL DEATH

Groups	*Individual Diseases*	*Number*	*Percentage of Group*	*Percentage of Total (2,030)*
Heart and Aorta 912 Cases (44.9%)	Coronary artery disease	617	67.7	30.4
	Syphilitic aortitis	107	11.7	5.3
	Valvular disease	83	9.2	4.1
	Cardiac hypertrophy	35	3.8	1.7
	Spontaneous rupture of aorta	25	2.7	1.2
	Others	45	4.9	2.2
Respiratory 460 Cases (23.1%)	Lobar pneumonia	176	37.6	8.7
	Bronchitis, bronchopneumonia	133	28.4	6.5
	Pulmonary tuberculosis	68	14.5	3.4
	Pulmonary embolism and infarction	31	6.7	1.6
	Others	60	12.8	2.9
Brain and Meninges 367 Cases (17.9%)	Cerebral hemorrhage	110	30.4	5.4
	Subarachnoid hemorrhage	93	25.7	4.6
	Cerebellar hemorrhage	11	3.0	0.6
	Pontine hemorrhage	11	3.0	0.6
	Cerebral thrombosis and embolism	27	7.5	1.3
	Meningitis	38	10.6	1.9
	Brain tumor	29	8.0	1.4
	Others	43	11.8	2.1
Digestive and Urogenital		190		9.7
Miscellaneous		90		4.4

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